COMPREHENSIVE ANALYSIS OF ORGANOPHOSPHOROUS POISONING IN POISON CENTRE, GOVERNMENT GENERAL HOSPITAL, CHENNAI

Dissertation Submitted For

M.D. DEGREE IN GENERAL MEDICINE

BRANCH - I

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MARCH 2007

CERTIFICATE

Certified that this dissertation entitled **"COMPREHENSIVE ANALYSIS OF ORGANOPHOSPHOROUS POISONING IN POISON CENTRE, GOVERNMENT GENERAL HOSPITAL, CHENNAI"** is a bonafide work done by **DR.N.EZHILAN,** post graduate student of Internal Medicine, Institute of Internal Medicine, Madras Medical College, Chennai - 600 003, during the academic year 2004-2007.

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DECLARATION

I solemnly declare that this dissertation entitled **"COMPREHENSIVE ANALYSIS OF ORGANOPHOSPHOROUS POISONING IN POISON CENTRE"** was done by me at Madras Medical College and Govt. General Hospital, during 2004-2007 under the guidance and supervision of **Prof.C.Rajendiran, M.D**. This dissertation is submitted to the Tamil Nadu Dr.M.G.R. Medical University towards the partial fulfillment of requirements for the award of M.D. Degree in General Medicine (Branch - I).

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CONTENTS

ABBREVIATIONS

ACH – ACETYL CHOLINE

AcHE-ACETYL CHOLINESTERASE

ABG- ARTERIAL BLOOD GAS ANALYSIS

CK - CREATINE KINASE

CK-MB-CREATINE KINASE MB FRACTION

ECG- ELECTROCARDIOGRAM

GIT- GASTROINTESTINAL TRACT

GBS- GUILLAIN BARRE SYNDROME

GGH- GOVERNMENT GENERAL HOSPITAL

IMS INTERMEDIATE SYNDROME

LDH- LACTATE DEHYDROGENASE

PAM- PRALIDOXIME

INTRODUCTION

NECESSITY IS THE MOTHER OF INVENTION

Humans in this modern world have made numerous inventions for their survival and existence. Organophosphorous compounds are one of those creations. Being developed as pesticides, now they form important ingredient of weapons of mass destruction. In spite of increased dividends in food production and vector control, these compounds have resulted in serious ill effects to man and his ecosystem.

More than 225 groups of organophosphorous pesticides are being marketed world wide. These pesticides are misused as an important commodity for deliberate self harm in developing world. Self poisoning with agricultural pesticides is an important cause of mortality in many rural areas(1) Case fatality rate of organophosphates may exceed 60% in third world countries.(1). They form the major group of suicidal poisoning in developing countries because of their easy availability, cheap cost and their toxic nature. The developed nations have also renewed their interest in these compounds because of its potency as weapons of mass destruction. In this current scenario medical management of acute opc poisoning is having lacunae in evidence based treatment protocols and research tools that would reduce mortality. This calls for an urgent comprehensive analysis of opc poisoning to promote a preventive, educational and management programme in countries like India where economy is predominantly based upon agricultural sector . (1)

REVIEW OF LITERATURE

HISTORY

In the era of industrial revolution many organophosphorous compounds were synthesized. As early 1854 CLERMONT prepared tetra ethyl pyrophosphate (TEPP) OPC made its mark in modern chemistry when LANGE and KRUEGER recorded the synthesis of di-methyl di-ethyl phosphor fluoridates in 1932(2). They observed that inhalation of these compounds produced blurring of vision and choking sensation. But opc as pesticides were produced by a group of German scientists led by Gerhard Schrader, FarbenFebriken and Bayer AG 1937.The possibilities of potential chemical warfare with these agents were explored by Nazis in World War II. Indeed Sarin (isopropyl methyl phosphono fluoridate) was used by Iraq against Kurdish rebels in villages of north IRAQ. (3)The residues of Sarin were still found in analysis of the soil. In 1944 SCHRADER synthesized parathion which was widely used as a pesticide.In1870 FRASER developed atropine as an antidote to physostigmine. COLLOMP in 1949 experimented atropine against muscarinic effects of nerve gas .In 1955 Davies introduced oximes and I.B WILSON confirmed its usefulness in opc acute poisoning .NAMBA for the first time used pralidoxime in his victims of opc poisoning in 1956. Lallement studied GK-11 an anti Glutamimmetic drug as a neuro protective agent in OPC in 1997.In 1998 adenosine receptor antagonist role was studied in opc necessitating further studies.

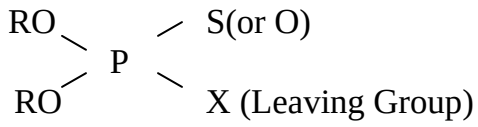
TABLE 1 CLASSIFICATION AND THEIR STRUCTURE

Sl. No.	Common Name	Trade Name
1.	Acephate	Asataf, Orthene, Starthene
2.	Chlorpyrifos	Dursban, Durmet, Lorsban
3.	Dichlorvas	Noovan
4.	Dimethoate	Rogar, Tara 909, Fosfamid
5.	Fenitrothian	Surmunion, Nitrophos
6.	Fenthion	Baycid, Baytex
7.	Malathion	Cythion, Chemathion
8.	Methyl Parathion	Metacid, Folitav, Paramox, Metaphos
9.	Monocrotophos	Monocron, Nivacron, Luphos
10.	Phorate	Thimet, Pempart
11.	Parathion	Folidol, Ekatox
12.	Phosphomidon	Dimecron, Famfos
13.	Quinalphos	Ekalux

GENERAL CHEMICAL STRUCTURE

Organophosphorous compounds are basically esters of phosphoric acid or of phosphorothioic acids (4).The R denotes either ethyl or methyl group. The

organothiophosphates which contains double bonded sulphur group are converted into organophosphates in the liver.Phosphonate contains an alkyl(R-) in place of one alkoxy group (RO-). The X is called the leaving group and is the principal metabolite for species identification. (5).



KINETICS

The kinetics of each group are highly dependent upon many factors such as route of administration such as ingestion, injection ,inhalation ,transdermal and transmucosal exposure, distance from target organs, local versus systemic metabolism and activation, route of elimination, endogenous hydrolysis and consumption of the compound by non specific esterases. Each group has its chemical structure ,R- groups attached to the sulphur, carbon, or phosphorus entity, tightness of the bond to the central atom and the inherent affinity to cholinesterase.(6) After absorption the chemicals are equally distributed in all tissues but predominantly in liver and the renal. Lipophilic compounds reach maximum concentration in neural and other lipid rich tissues. Plasma half life after single dose administration depends upon the type of opc and route of exposure and it may range from few minutes to few hours. Metabolism occurs mainly by three ways namely oxidation, hydrolysis by esterases and transfer of portion of molecule to glutathione. Urinary and faecal excretion occurs in 48hours where in 80 -90% of the compound is eliminated.(7).Most of the agents show some symptoms and

signs within six to ten hours(8) with the exception of fat soluble compounds where it may take several days to weeks to manifest because the substance must be leached out of the fat. Some opc have to be activated to active toxic state (hepatic activation of parathion to paraxon).Studies reveal that these residues may remain for days to week even after treatment.(8)

HIGHLY TOXIC

FOLIDOL, DIMECRON, TRITHION, CELATHION, SYSTOX

MODERATELY TOXIC

BAYTEX, TIC20, ABATE, FINIT (9)

LOW TOXIC

MALATHION, DICHLORVOS (10)

LIPHOPHILIC

TRITHION, BAYTEX, FENTHION

MECHANISM OF ACTION

Acetylcholine (ACh) is the neurotransmitter released at all postganglionic parasympathetic nerve endings and at the synapses of both sympathetic and parasympathetic ganglia. It is also released at the skeletal muscle myoneural junction, and serves as a neurotransmitter in the central nervous system. ACh is hydrolyzed by acetyl cholinesterase into two fragments: acetic acid and choline.

Acetyl cholinesterase is present in two forms: True acetyl cholinesterase which is found primarily in the tissues and erythrocytes, and pseudo cholinesterase which is found in the serum and liver.

Organophosphorous compounds are acid-transferring inhibitors of cholinesterase. They cause cholinesterase to become firmly (and sometimes irreversibly) phosphorylated. This means that the action of cholinesterase will be inhibited. Cleavage of the carbon-enzyme bond from ACh is complete in a few microseconds. However, the breaking of the phosphorus-enzyme bond requires a period varying from 60 minutes to several weeks, depending on the organophosphorous compound involved.

Reactivation of the inhibited enzyme may occur spontaneously. The rate of reactivation will depend on the species, the tissue, and the chemical group attached to the enzyme. Reactivation may be enhanced by hydrolysis of the acid-radical-enzyme through the use of oximes (i.e. reactivating agents). Response to reactivating agent's declines with time; this process being caused by "ageing" of the inhibited enzyme. Ageing is probably the result of the loss of one alkyl or alkoxy group, leaving a much more stable acetyl cholinesterase. The aged phosphorylated enzyme cannot be reactivated by oximes.

Accumulation of acetylcholine causes over stimulation of both muscarinic and nicotinic receptors, and subsequently disrupts the transmission of nerve impulses in both the peripheral and central nervous system. (11)

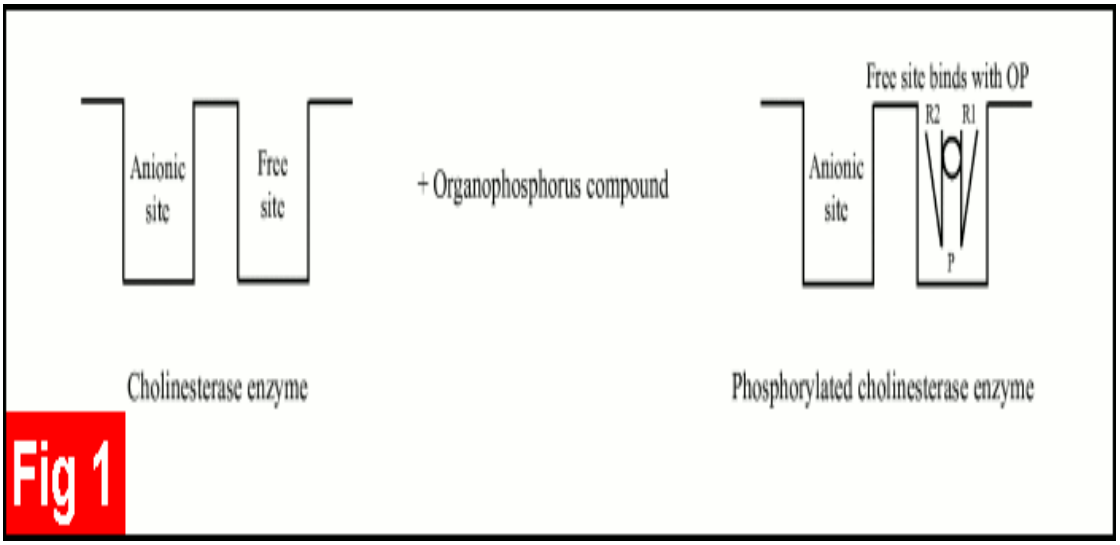


Fig 1

Most of these opc do not possess a positive charge, hence they react with esteratic site but not with anionic site. Splitting of the acid group the occurs.

The bond between phosphorous and esteratic site (free site) is more stable than the bond between carbon atom of acetyl choline and the same site. Thus blocking of the active site and consequent inactivation of enzymes results in accumulation of acetylcholine at cholinergic sites .Pseudo cholinesterase is a less specialized enzyme as it lacks an anionic site in a position that specially adapts it to react with acetylcholine. It does however react with acetyl choline, albeit, more slowly and also with a wide range of other esters

BIOLOGICAL INTERACTIONS OF OPC (12)

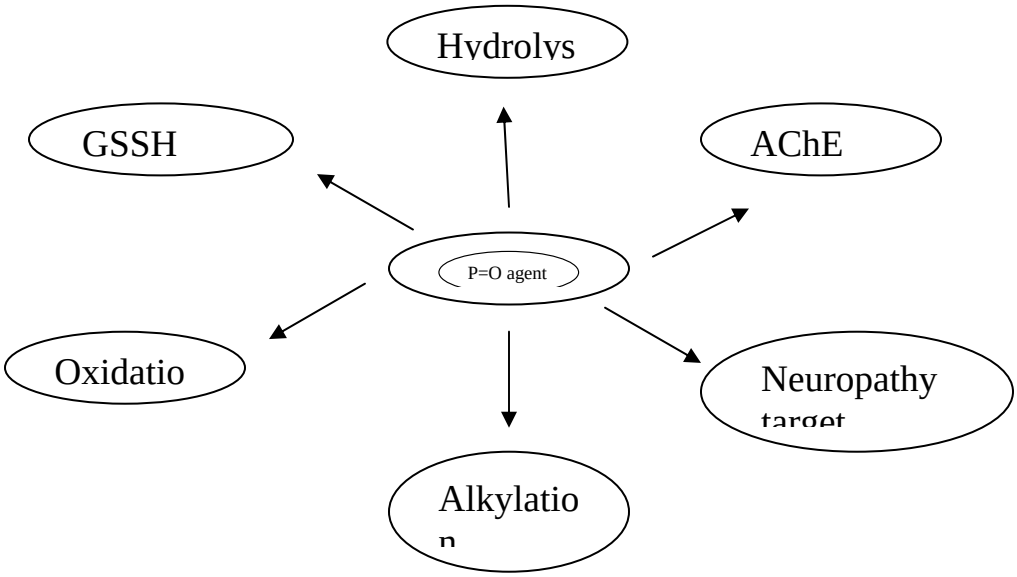


Fig.2

CLINICAL FEATURES

The clinical features depend upon the end points where sustained cholinergic stimulation takes place namely

a. Post ganglionic parasympathetic hollow end organ (muscarinic)

b. Sympathetic and parasympathetic ganglionic and somatic neuro muscular junction(nicotinic)

c. Central nervous system affection(13)

Following exposure to organophosphorous compounds, the toxic features are usually obvious within 30 minutes to 3 hours. This may be delayed in some cases depending on the rate and amount of systemic absorption. The majority of

patients give a history of intentional or accidental ingestion of organophosphorous compounds. Toxicity is produced by the rapid absorption of the compound through the gastrointestinal, respiratory tracts and skin.

The clinical symptoms and signs are non-specific and will depend on the specific agent, the quantity and the route of entry. Some patients present with vomiting, diarrhea and abdominal pain, whilst others may be unconscious on arrival at the hospital. A high index of suspicion is therefore needed to make an early diagnosis. Early cases present predominantly with parasympathetic over-activity, and a characteristic garlic smell. The end result may be a multi-system manifestation involving the gastrointestinal, respiratory, and cardiovascular and nervous systems, as well as involvement of skeletal muscle, other organs and metabolic effects such as hypo or hyperglycemia. Most fatalities occur within 24 hours and those who recover usually do so within 10 days.

CARDIAC MANIFESTATIONS

The commonest cardiac manifestations following poisoning are hypotension (with warm, dilated peripheries), and bradycardia. Patients seldom present with tachycardia and hypertension due to predominant nicotinic receptor blockade. Cardiac manifestations are often the cause of serious complications and fatality. (14).

Table 2. Symptoms and signs of organophosphorous poisoning		
Muscarinic receptors	**Nicotinic receptors**	**Central receptors**
Cardiovascular • Bradycardia • Hypotension **Respiratory** • Rhinorrhoea • Bronchorrhoea • Bronchospasm • Cough **Gastrointestinal** • Nausea/vomiting • Increased salivation • Abdominal cramps • Diarrhea • Faecal incontinence **Genitourinary** • Urinary continence **Eyes** • Blurred vision • Increased lacrimation • Miosis **Glands**	**Cardiovascular** • Tachycardia • Hypertension **Musculoskeletal** • Weakness • Fasciculation • Cramps • Paralysis	**General effects** • Anxiety • Restlessness • Ataxia • Convulsions • Insomnia • Dysarthria • Tremors • Coma • Absent reflexes • Respiratory depression • Circulatory collapse

• Excessive salivation		

The mechanism of cardiac toxicity is unclear and the following has been postulated:

- A direct toxic effect on the myocardium
- Over activity of cholinergic or nicotinic receptors causing hemodynamic alteration
- Hypoxia
- Acidosis
- Electrolyte abnormalities
- High dose atropine therapy (used as treatment for organophosphate poisoning).

RESPIRATORY MANIFESTATIONS

Respiratory manifestations of acute organophosphorous poisoning include bronchorrhoea, rhinorrhoea, bronchospasm and laryngeal spasm. This is due to the action of the organophosphate on muscarinic receptors. The integrity of the airway may be compromised by excessive secretions. The nicotinic effects lead to weakness and subsequent paralysis of respiratory and oropharyngeal muscles. This

increases the likelihood of both airway obstruction and aspiration of gastric contents. Finally, central neurological depression may lead to respiratory arrest.

GASTROINTESTINAL MANIFESTATIONS

Symptoms resembling gastroenteritis such as vomiting, diarrhea and abdominal cramps are the first to occur after oral ingestion of an organophosphorous compound.

NEUROLOGICAL MANIFESTATIONS

A large number of patients, following acute exposure to organophosphorous compounds, require prolonged ventilatory support in the intensive care unit due to neuromuscular weakness. The neurological manifestations have therefore been a primary focus of interest. There has been an emphasis on reducing the incidence of neuro-muscular respiratory failure. Three different types of paralysis are recognized based largely on the time of occurrence and their differing path physiology:

- Type I paralysis or acute paralysis
- Type II paralysis or Intermediate syndrome
- Type III paralysis or Organophosphate- induced delayed polyneuropathy

Type I paralysis or acute paralysis is seen during the initial cholinergic phase. This is when large numbers of both muscarinic and nicotinic receptors are occupied by acetylcholine, leading to persistent depolarization at the

neuromuscular junction. Clinical features include muscle fasciculation, cramps, twitching and weakness. At this stage the patient may require ventilatory support due to the weakness of the respiratory muscles leading to respiratory depression and arrest.

Type II paralysis or Intermediate syndrome. This was first described in 1974 by Wadia et al (14)as type II paralysis and subsequently termed "The Intermediate Syndrome" by Senanayake. This syndrome develops 24-96 hours after the poisoning. Following recovery from the acute cholinergic crisis, and before the expected onset of delayed neuropathy, some patients develop a state of muscle paralysis. The cardinal feature of the syndrome is muscle weakness affecting the proximal limb muscles and neck flexors. There is a relative sparing of the distal muscle group. One of the earliest manifestations in these patients is the inability to lift their head from the pillow (due to a marked weakness in neck flexion). This is a useful test to establish whether or not a patient is likely to develop respiratory muscle weakness. Of the cranial nerves, those supplying the extra-ocular muscles are mostly involved, with a lesser effect on VII and X. This syndrome persists for about 4-18 days and most patients will survive unless infection or cardiac arrhythmias complicate the course.

Type III paralysis or organophosphate- induced delayed polyneuropathy (OPIDP) is a sensory-motor distal axonopathy that usually occurs after ingestion of large doses of an organophosphorous compound (15-17)The neuropathy presents as weakness and ataxia following a latent period of 2-4 weeks. Initial stimulation causes excitatory fasciculation, which then progresses to an inhibitory

paralysis. The cardinal symptoms are distal weakness of the hands and feet. This is often preceded by calf pain, and in some cases, parasthesia of the distal part of the limbs. Delayed CNS signs include tremor, anxiety and coma.

OTHER EFFECTS OF OPC MAY INCLUDE

- Neuropsychiatric effects: Impaired memory, confusion, irritability, lethargy, psychosis, and chronic organophosphate-induced Neuropsychiatric disorders have been reported. The mechanism is not proven.(18)

- Extra pyramidal effects: These are characterized by dystonia, cogwheel rigidity, and parkinsonian features (basal ganglia impairment after recovery from acute toxicity).

- Other neurological and/or psychological effects: Guillain-Barré–like syndrome and isolated bilateral recurrent laryngeal nerve palsy are possible.(19)

- Ophthalmic effects: Optic neuropathy, retinal degeneration, defective vertical smooth pursuit, myopia, and miosis (due to direct ocular exposure to organophosphates) are possible.

- Ears: Ototoxicity is also possible(20).

MODIFIED DREISBACH' CLINICAL CRITERIA – KARNIT(9)

GRADE I - Mild symptoms related to portal of entry.

Nausea, vomiting in case of ingestion

Cough, burning sensation in the chest in case of inhalation Mild systemic symptoms like headache, dizziness, weakness

GRADE II - Moderate systemic intoxication

Abdominal pain, diarrhea in case of ingestion.

Tightness in chest, difficulty in breathing in case of inhalation

Salivation,lacrimation, sweating, papillary changes. Bradycardia, confusion, tremor, restlessness.

GRADE III - Severe systemic intoxication

Respiratory depression, generalized weakness

Cyanosis, peripheral circulatory failure,

convulsions coma.

DIAGNOSTIC CRITERIA (13)

- **INVESTIGATORY MODALITES: ESTIMATION OF CHOLINEESTERASE LEVELS:** Organophosphate (OP) toxicity is a clinical diagnosis. Confirmation of organophosphate poisoning is based on the measurement of cholinesterase activity; typically, these results are not readily available. Although RBC and plasma (pseudo) cholinesterase levels

can both be used, RBC cholinesterase correlates better with CNS acetyl cholinesterase (AChE) and is, therefore, a more useful marker of organophosphate poisoning.

- Measurement of RBC and plasma cholinesterase levels prior to treatment with pralidoxime (2-PAM). Monitoring serial levels can be used to determine a response to therapy.
- RBC AChE represents the AChE found on RBC membranes, similar to that found in neuronal tissue. Therefore, measurement more accurately reflects nervous system OP AChE inhibition.
- Plasma cholinesterase is a liver acute-phase protein that circulates in the blood plasma. It is found in CNS white matter, the pancreas, and the heart. It can be affected by many factors, including pregnancy, infection, and medical illness. Additionally, a patient's levels can vary up to 50% with repeated testing.
- RBC cholinesterase is the more accurate of the 2 measurements, but plasma cholinesterase is easier to assay and is more readily available.

- Cholinesterase levels do not always correlate with severity of clinical illness.
- The level of cholinesterase activity is relative and is based on population estimates. Neonates and infants have baseline levels that are lower than

adults. Because most patients do not know their baseline level, the diagnosis can be confirmed by observing a progressive increase in the cholinesterase value until the values plateau over time.

- Falsely depressed levels of erythrocyte cholinesterase can be found in pernicious anemia, hemoglobinopathies, use of antimalarial drugs, and oxalate blood tubes.

- Falsely depressed levels of plasma cholinesterase are observed in liver dysfunction, low-protein conditions, neoplasia, hypersensitivity reactions, use of certain drugs (succinylcholine, codeine, and morphine), pregnancy, and genetic deficiencies.

- Other laboratory findings include leukocytosis, hemoconcentration, metabolic acidosis, hyperglycemia, hypokalemia, and hypomagnesemia.

IMAGING STUDIES

A chest radiograph may reveal pulmonary edema but typically adds little to the clinical management of a poisoned patient. Electrocardiographic manifestations include prolonged Q-Tc intervals, elevation of the ST segment, inverted T waves and a prolonged PR interval. There may also be rhythm abnormalities such as sinus bradycardia, ventricular extra- systoles, ventricular tachycardia and fibrillation. Ludomirsky et al described three phases of cardiac toxicity following organophosphate poisoning:

- **Phase I**: A brief period of increased sympathetic tone

- **Phase II**: A prolonged period of parasympathetic activity including AV node blockade

- **Phase III**: Q-T prolongation followed by torsades de pointes, ventricular tachycardia and ventricular fibrillation (35)

THERAPEUTIC CONSIDERATIONS

Medical Care: Airway control and adequate oxygenation are paramount in organophosphate (OP) poisonings. Intubations may be necessary in cases of respiratory distress due to laryngospasm, bronchospasm, bronchorrhoea, or seizures. Immediate aggressive use of atropine may eliminate the need for intubation.(21) Succinylcholine should be avoided because it is degraded by acetyl cholinesterase (AChE) and may result in prolonged paralysis.

- Continuous cardiac monitoring and pulse oximetry should be established; an ECG should be performed. Torsades de Pointes should be treated in the standard manner. The use of intravenous magnesium sulfate has been reported as beneficial for organophosphate toxicity.(22) The mechanism of action may involve acetylcholine antagonism or ventricular membrane stabilization.

- Remove all clothing and gently cleanse patients suspected of organophosphate exposure with soap and water because organophosphates are hydrolyzed readily in aqueous solutions with a high pH. Consider clothing hazardous waste and discard accordingly.

- Health care providers must avoid contaminating themselves while handling patients. Use personal protective equipment, such as neoprene or nitrile gloves and gowns, when decontaminating patients because hydrocarbons can penetrate non polar substances such as latex and vinyl. Use charcoal cartridge masks for respiratory protection when decontaminating patients who are significantly contaminated.

- Irrigate the eyes of patients who have ocular exposure using isotonic sodium

If ingestion occurred within 30 to 60minutes placement of nasogastric tube and administration of activated charcoal in a dose, 1g/kg orally. Cathartics are contraindicated because of electrolyte imbalance. (23)

Atropine administration: 3-5mg rapid intravenous should be given to reach effective atropinisation. The adequate atropinisation is gauged by five parameters.

1. Pulse rate >85/min
2. Systolic blood pressure >80mmHg
3. Absence of lung crepitations
4. Dry axilla
5. No constricted pupils(9)

Then after three to five minutes if the parameters are not attained double the initial dosing. Atropine should be given in doubling dose pattern till adequate atropinisation.

Maintenance of atropinisation: 10 -20% of the bolus dose should be given as infusion in100ml normal saline and the parameters are assessed every 15minutes.If there is inadequate atropinisation superimposed bolus in the dosage of 3-5mg should be given. Atropine should be tailored down hourly for six hours and then every two to three hours for the next 24hrs.Meticulous watch for atropine toxicity such as agitation, confusion, retention of bladder, hyperthermia, ileus and tachycardia should be done.

OXIMES: PRALIDOXIME (2-PAM OR PROTO PAM) (24)

Cholinesterase reactivation

Oximes are nucleophilic agents that re-activate the phosphorylated acetyl cholinesterase by binding to the organophosphorous molecule. The use of oximes in acute organophosphorous poisoning has been a controversial subject for the last two decades as there have been very few randomized controlled trials that have addressed the role of pralidoxime (PAM).

Pralidoxime has three main actions

- A direct reaction converting the organophosphate to a harmless compound.

- A transient reaction protecting the enzyme from further inhibition.
- Reactivation of the inhibited alkyl phosphorylated enzyme to free the active unit (if given early enough)

The reactivating action of pralidoxime is most marked at the nicotinic skeletal neuromuscular junction. It does not reverse the muscarinic manifestations of organophosphorous poisoning. Pralidoxime should be started as early as possible to prevent permanent binding of the organophosphate to acetyl cholinesterase. Once this has occurred, receptor regeneration is required to allow recovery. The recommended dose of pralidoxime in organophosphorous poisoning is 1 gram, by intravenous injection, every 6-12 hour in adults (maximum dose 12g/24 hours) and 25-50mg/kg in children. Pralidoxime should be continued until adequate spontaneous ventilation is achieved by the patient. The effective plasma concentration is 4mg/litre and the patient should show signs of improvement 10-40 minutes after its administration. Plasma and pseudo cholinesterase levels should ideally be monitored during treatment. Side effects of pralidoxime include drowsiness, visual disturbances, nausea, tachycardia and muscle weakness, so treatment should be reserved for potentially fatal cases.

PREVENTION AND EDUCATION

Improved regulation of the availability of pesticides, strict regulation of vendors, and modifications in packaging of pesticides may all help reduce the use of organophosphates as poisons. Adequate provision of information to the public, regular training of health care providers, better availability of drugs / antidotes and

the establishment of poison information centers will facilitate in reducing the morbidity and mortality related to organophosphorous poisoning. Insecticides should be kept out of reach of children, to prevent accidental poisoning. During agricultural spraying, proper precautions should be taken to prevent inhalation and accidental ingestion of the substance. The greatest incidence of organophosphorous poisoning was reported from Japan where there were 19,436 cases over a period of 17 years (1953-1969).WHO used data from 19 countries and reported approximately5, 00,000cases of pesticide poisoning annually. Of these 99% belong to third world countries(24).In1981 the estimate was 75,000 cases annually and rose to 3million in 1983 and majority were under the age of 30(36). Pesticide poisoning contributes more than forty percent of cases in Poison Centre GGH Chennai. The mortality rate due to this poison is 42.29% (case register2001-2004). The victims are farmers of rural South India. Since only limited studies are available in analyzing the predictors of mortality in this most common form of agricultural poison, the outcome analysis of the predictors form the basis of the thesis

OBJECTIVES

1. To describe the epidemiology of organophosphorous poisoning in poison centre Government General Hospital Chennai.

2. To study the clinical profile of organophosphorous poisoning in poison centre Government General Hospital Chennai

3. To analyze the epidemiological and clinical factors in correlation to severity and outcome of organophosphorous poisoning in poison centre Government General Hospital Chennai.

4. To identify prognostic indicators from biochemical parameters (renal function test, liver enzymes, arterial blood gas analysis, enzymes such as creatine kinase, creatine kinase mb fraction, serum amylase and lactate dehydrogenase,) to predict the severity, outcome and the need of ventilatory support.

5. To asses the clinical severity and outcome of organophosphorous poisoning and correlate the same with pseudo cholinesterase levels

6. To do outcome analysis of clinical and biochemical parameters in mechanically ventilated patients .

7. To compare the effectiveness of low dose versus high dose administration of pralidoxime in organophosphorous poisoning in relation to the need of ventilatory support and mortality.

MATERIALS AND METHOD

SETTING: This study was conducted in the Poison centre GGH Chennai in collaboration of Institute of Internal Medicine and Institute of Biochemistry. It was a cross sectional prospective study done during the period from September2005-September2006. 87patients with history and clinical features suggestive of organophosphorous poisoning were selected irrespective of age and sex. 46 age and sex matched controls from normal population (patient attendants) were studied for biochemical markers.

EXCLUSION CRITERIA

1. Patients with other pesticide poisoning were excluded (eg., organo carbamate organochlorous compounds) by clinical features and confirmed by thin layer chromatographic analysis of gastric aspirate.

2. Patients with other poisoning such as oleander, oduvanthazai , and drug over dosage(nicotine replacements, inocybe clitocybe, pilocarpine, opioids,phenothiazines,bethanechol.etc)known to mimic the clinical picture of organophosphorous poisoning were excluded.

3. Patients with known medical illness such as neuromuscular disorders like myasthenia gravis or muscular dystrophy, hypokalemic periodic paralysis and conditions known to alter biochemical parameters were excluded.

- Patients with known history of exposure to organophosphorous compounds were taken into consideration. The reliability on exposure was reinforced by definite history from the patients and their attendants. The container from which the poison where consumed were studied for the type and the quantity estimated. Each patient registered for the study went through detailed clinical evaluation as per the proforma.The cases were divided into three groups as mild moderate and severe by modified DREISBACH criteria. All patients underwent baseline laboratory investigations. The gastric aspirate was analyzed by thin layer chromatography method for the detection of poison.

All patients underwent renal function test, arterial blood gas analysis, ecg chest roentogram and sonogram of the abdomen.

Serum AChE were measured on day 1 3 and 5.

The other biochemical markers such as liver enzymes, CK,CK-MB,LDH and amylase were taken on day1.

BI0CHEMICAL MARKERS AND THE METHODS EMPLOYED- (KITS)

1.CHOLINESTERASE	-	KINETIC COLOIMETRIC METHOD(26)
2.SGOT (AST)	-	UV KINETIC METHOD (27)
3.SGPT	-	(MODIFIED IFCC METHOD)- (28)

4.ALKALINE PHOSPHATASE	-	PNPP METHOD(29)
5.ALBUMIN	-	BCG METHOD(30)
6. CK	-	UV KINETIC METHOD(31)
7.AMYLASE	-	CNP – G3 METHOD(32)
8. LDH	-	UV KINETIC METHOD(28)

On treatment aspect, average total dose of atropine administered per patient was calculated in mg. All patients in the study were given pralidoxime . They were sub divided into two groups –low dose and high dose based upon the total grams per day(<4gm/dayand >4gm /day)(33)

- Ventilatory support was considered in patients with following parameteres

a. RR >35/min

b. Apnea or obvious hypoventilation

c. Persistent cyanosis,excessive secretions,depressed level pf unconsciousness,inability to protect the air way(34)

d. PaO2 < 60 mmHg, FiO2 >0.6

PaCO2 > 50 mmHg, pH <7.2

Mechanical ventilation was performed with assist control mode and simv either as volume or pressure control. Positive end expiratory pressure was titrated to keep SaO_2 above 94% with 40% FIO_2. Weaning was performed using either T-

tube trials or pressure support weaning. All patients were monitored meticulously and vital signs assessed till the outcome.

STATISTICAL METHOD

The chi-square test was used for statistical analysis. Logistic Regression analysis was run to identify the parameters that would predict the clinical severity, need for mechanical ventilation and the outcome. Data are presented as mean ± standard deviation.

Detailed evaluation of each patient was made. Each variable in the pro-forma was correlated with severity and mortality.

RESULTS

Epidemiological Pattern of OPC in Poison Centre, Govt. General Hospital

TABLE 3 - Age Distribution

Sl.No.	Age Group in years	Frequency(n)	Percentage
1.	<= 20	17	19.54
2.	21-30	40	45.98
3.	31-40	15	17.24
4.	> 40	15	17.24
	Total	87	100.00

Majority of the patients were in the 21 to 30 age group. The number of people between the age group 20 to 40 accounts for 55 out of 87 cases.

TABLE 4 – Age Distribution and Outcome

Sl.No.	Age Group in years	Outcome	
		Discharge	Death
1.	<= 20	14	3
2.	21-30	33	7
3.	31-40	10	5
4.	> 40	8	7
	Total	65	22

The correlation between the age group and the outcome was not statistically significant (P value – 0.11)

Table.5 Sex Distribution

Sl.No.	Sex	Frequency(n)	Percentage
1.	Male	76	87.36
2.	Female	11	12.64

Incidence of OPC was more in males when compared to females in our series.

Table.6 - Occupation

Sl.No.	Occupation	Frequency(n)	Percentage	Expired
1.	Agriculture	40	45.98	9
2.	Unskilled Labour	37	42.53	9
3.	Others	10	11.49	4

More than 80 percent of the cases of OP poisoning were among agriculturalists and unskilled labourers. The death rate was also more among these groups.

Locality – Distance from the Poison Centre, Govt. General Hospital in Kilo Meters.

Table 7 – Locality

Sl.No.	Locality (kms)	Frequency(n)	Percentage
1.	<= 100	40	45.98
2.	> 100	47	54.02

Table 8 - Type of Poison consumed

Sl.No.	Type of Poison consumed (kms)	Frequency(n)	Percentage
1.	CHLORPYIFOS	6	6.90
2.	DIMECRON	26	29.89
3.	QUINALPHOS (EKALUX)	3	3.45
4.	FENTHION (BAYTEX)	2	3.45
5.	HINOXAN	3	2.30
6.	MALATHION (CHEMATHION)	2	2.30
7.	METHYL PARATHION (METAPHOS)	1	1.15
8.	MONOCROTOPHOS	2	2.30
9.	PARATHION (FOLIDOL, EKATOX)	30	34.49
10.	PHORATE	3	3.45
11.	SYSTOX	1	1.15
12.	TRIPHOS	6	6.90
	Total	87	100.00

Most of the patients in this series consumed parathion (n=30) and Dimecron (n=26). But the type of poison does not contribute both to severity and mortality.

Table.9 - Route Of Exposure

Sl.No.	Route of Exposure	Frequency(n)	Percentage
1.	Ingestional	75	86.2
2.	Inhalational	10	11.5
3.	Topical	2	2.3

Ingestional exposure was more common among in the series(86.2%) and most of the patients in this entity fell under the severe grade of Dreisbach's criteria (P value = 0.03).

Intention Of Poison: Suicidal (75) - Accidental (12)

Table.10 Duration of stay in hospitals

Sl.No.	Duration of Stay in Hospitals (in days)	Frequency(n)	Percentage
1.	<= 5	38	43.68
2.	6-10	32	36.78
3.	> 10	17	19.54
		87	100.00

The mean duration of stay in the hospital is 7.25 days (SD 4.64)

Table 11 - Duration Of Hospital Stay Correlation With Clinical Severity-

Duration of Stay in Hospitals (in days)	Clinical Severity at admission		
	Mild	**Moderate**	**Severe**
0-5	n=9 23.7%	n=15 39.5%	n=14 36.8%
6-10	n=6 18.8%	n=14 43.8%	n=12 37.5%
> 10	0	0	n=17 100%

In this series of 87 cases, more severe grade of intoxication had longer duration of stay in the hospital (P value =0.0002)

Table 12 - Quantum of exposure

Sl.No.	**Quantity consumed (ml.)**	**Frequency(n)**	**Percentage**
1.	NA	25	28.74
2.	<=50	29	33.33
3.	51-100	19	21.84
4.	>100	14	16.09
	Total	87	100.00

The non availability of data in 25 patients was due to two reasons. 1. 12 cases had inhalataional and topical forms of exposure so the quantity cannot be ascertained 2. In 13 cases reliable information regarding the quantity of consumption was not known. The average quantity of consumption in this series amounts to 101.58ml.

Table 13 – Quantity of Consumption and Clinical Severity

Quantity of Consumption (ml.)	Clinical Severity at Admission		
	Mild	**Moderate**	**Severe**
< =50	n=5 17.2%	n=13 44.8%	n=11 37.9%
50-100	n=4 21.1% |	n=2 10.5% |	n=13 68.4%
>100		n=2 14.3%	n=12 85.7%

Patients who have consumed more than 100 ml. of OPC have higher grade of severity (P value = 0.004). The quantity consumed had no relation to the mortality rate. 21 cases had OPC mixed with alcohol. Two cases consumed OPC mixed with phenol and kerosene.

Table.14 - Onset Of Symptoms After Exposure

Sl.No.	Time of onset of Poisoning (Mins.)	Frequency(n)	Percentage
1.	NA	1	1.15
2.	<=30	40	45.98
3.	31-60	36	41.38
4.	>60	10	11.49
	Total	87	100.00

Most of the patients had their initial symptom of intoxication between 30 minutes to one hour.

PERIOD INTERVAL FOR INITIATION OF TREATMENT

a) Initiation of First Aid (Gastric Lavage/activated charcoal)

Table 15 –Initiation Of First Aid

Sl.No.	Initiation of First aid (Hours.)	Frequency(n)	Percentage
1.	<=1	33	37.93
2.	1-2	32	36.78
3.	>2	22	25.29
	Total	87	100.00

Out of 87 patients 65 received first aid either at household or nearby medical facility within two hours.

b) Initiation of Atropine

Table.16 - Time of initiation of Atropine

Sl.No.	Time of initiation of Atropine (Hours.)	Frequency(n)	Percentage
1.	<=1	35	35.63
2.	1-3	38	43.68
3.	>3	18	20.69
	Total	87	100.00

c) Initiation of 2- PAM

Table 17 - Time Of Initiation Of 2-PAM

Sl.No.	Time of initiation of 2-P AM (Hours.)	Frequency(n)	Percentage
1.	NA	4	4.60
2.	<=1	27	31.03
3.	1-3	36	41.38
4.	>3	20	22.99
	Total	87	100.00

More than 60 percent of the cases in this series have reached nearest medical services within three hours to receive their initial doses of atropine and 2 PAM.

Time taken to reach poison centre from the time of consumption

Table 18 - Time taken to reach Poison Centre

Sl.No.	Time taken to reach Poison Centre, GGH (Hours.)	Frequency(n)	Percentage
1.	NA	2	2.30
2.	<=5	30	34.48
3.	6-10	29	33.33
4.	>10	26	29.89
	Total	87	100.00

The mean duration to reach poison centre from the time of consumption - 9.99 hours.

Table 19 - Time interval to reach Poison Centre and Clinical Severity

Time interval to reach Poison Centre, GGH.(Hours)	Clinical Severity at Admission		
	Mild	**Moderate**	**Severe**
<=5	n=7 23.3%	n=10 33.3%	n=13 43.3%

	6-10	n=2 6.9% |	n=8 27.6% |	n=19 65.5%
	>10	n=4 15.4%	n=11 42.3%	n=11 42.3%

65 cases in the series were referred cases from other medical services. Patients reaching poison centre more than six hours after consumption came under severe grade of poisoning (P value = 0.02). The time interval between initiation of first aid atropine and P2 AM did not have statistically significant correlation with outcome.

SYMPTOM ANALYSIS

60 cases in the study presented with gastro intestinal symptoms (68 %) such as nausea, vomiting, cramps and diarrhoea. 47 cases had central Nervous system manifestations, out of which 26 presented with type 1 paralysis, 13 had seizures and 8 had IMS/Type 2 paralysis. Two cases with IMS had VII AND X cranial nerve affection. 27 cases had both GIT and nervous symptoms. Two cases presented predominantly with cardiac symptoms of chest pain and palpitations.

Table 20 - Cases Grouped According To Dreisbach Clinical Criteria At Admission

Sl.No.	Mild	Moderate	Severe

1.	15 (17.2%)	29 (33.3%)	43 (49.4%)

In this series of 87 cases, 49.4% of patients belong to the severe grade of poisoning.

1. Severity grading (Dreisbach clinical Criteria) correlation with outcome

Table 21- Severity Grading and outcome

		Outcome	
		Discharge	death
Severity Grading	Mild	n=14 93.3%	n=1 6.7%
	Moderate	n=26 89.7% |	n=3 10.3% |
	Severe	n=25 58.1%	n=18 41.9%

The mortality rate in the severe group was 41.9%. The correlation between severity grading and mortality as a very high statistical significance (P value =0.002)

2. **Severity grading (Dreisbach clinical Criteria) correlation to the need of ventilatory support**

Table 22 - Severity Grading and Ventilatory Management

		Ventilatory Management	
		No Support	**Ventilatory Support**
Severity Grading	Mild	n=15 100.0%	n=0
	Moderate	n=26 89.7% |	n=3 10.3% |
	Severe	n=4 9.3%	n=39 90.7%

(P value = 0.0000)

Out of 42 cases on mechanical ventilation, 39 cases were initiated on assist control mode and three were put on synchronized intermittent mandatory ventilation. (SIMV)

PROXIMAL MUSCLE GROUP INVOLVEMENT IN OPC

47 out of 87 cases had involvement of proximal muscles such as neck flexors, bulbar muscles and muscles of the shoulder and pelvic griddle. Out of this group, 8 cases developed IMS. The correlation of proximal muscle group affection was studied in relation to clinical severity, outcome and the need of

mechanical ventilation. These three variables studied had statistically significant relationship.

Table 23 - Proximal Muscle Group Involvement and Clinical Severity

Proximal Muscle Group Involvement		Clinical Severity		
		Mild	**Moderate**	**Severe**
	Yes	n=1 2.1%	n=13 27.7%	n=33 70.2%
	No	n=14 35.0% |	n=16 40.0% |	n=10 25.0%

(P value = 0.00001)

33 cases of proximal muscle group involvement had severe grade of poisoning.

Table 24 - Proximal Muscle Group Involvement and Ventilatory Management

Proximal Muscle Group Involvement		Ventilatory Management		
		No Support	**Assist control**	**SIMV**
	Yes	N=14 29.8%	n=30 63.8.7%	n=3 6.4%

	No	n=31 77.5%	n=9 22.5%	n=0

(P value = 0.0004)

Table 25 - Proximal Muscle Group Involvement and Outcome

Proximal Muscle Group Involvement		Outcome	
		Discharge	**Death**
	Yes	N=31 66.0%	n=16 34%
	No	n=34 85.0%	n=6 15.0%

(P value = 0.04170)

The mortality rate among the group which had proximal muscle involvement was 34 percent.

LABORATORY PARAMETERS

1. Average hemoglobin observed in these series – 13.2 g/dl/(SD =2.40)

2. Total WBC count had a range between 6500 and 27000 cells per cubic mm. and it had a mean value -14,038(S.D-5233.3)

3. Routine Bio-chemistry

Table 26 – Bio Chemistry Values

Sl.No.	Values	Mean	S.D. (+/-)
1.	Blood Sugar mg/dl.	103.7	32.26
2.	Urea mg/dl.	27.92	13.22
3.	Creatinine	|0.91	0.27
4.	Sodium	134	6.3
5.	Potassium	3.83	0.55
6.	Chloride	111.95	6.14

4. Liver Function Test (These parameters did not have any correlation with severity and outcome. The values of 87 patients are given below:

Table 27 - LFT

Sl.No.	Values	Mean	S.D. (+/-)
1.	SGOT IU/L	52.89	22.55
2.	SGPT IU/L	47.23	27.23
3.	Total Protein g/dl	6.54	0.48
4.	Albumin g/dl	3.60	0.70
5.	SAP IU/L	152.4	69.4

5. Arterial blood gas analysis

Table 28 - ABG

Sl.No.	Values	Mean	S.D. (+/-)
1.	ph	7.33	0.14
2.	PaCo2 mm/hg	43.31	13.17
3.	PaO2	87.05	16.28
4.	O2Sat	90.99	14.30
5.	Bicarbonate	23.44	5.58

Interpretation of arterial blood gas analysis revealed that 51 patients had normal pH. 28 patients had metabolic acidosis and 8 had respiratory alkalosis. The arterial blood gas analysis was studied in relation to severity of poisoning, need of ventilatory support of outcome. The results are as follows:

Table 29 – ABG & Clinical Severity

Arterial blood gas analysis (ABG)		Clinical Severity		
		Mild	**Moderate**	**Severe**
	Metabolic Acidosis	n=0	n=6 21.4%	n=22 78.6%
	Normal pH	n=15 29.4%	n=23 45.1%	n=13 25.5%

	Respiratory Alkalosis	n=0	n=0	n=8 100%

(P value = 0.0000)

Table 30 – ABG & Ventilatory Support

Arterial blood gas analysis (ABG)	Ventilatory Support			
		No support	**Assist control Mode**	**SIMV Mode**
	Metabolic Acidosis	n=5 17.9%	n=21 75%	n=2 7.1%
	Normal pH	n=40 78.4%	n=11 21.6%	n=0
	Respiratory Alkalosis	n=0	n=7 87.5%	n=1 12.5%

(P Value = 0.0000)

Table 31 – ABG & Outcome

Arterial blood gas analysis (ABG)	Outcome		
		Discharge	**Death**
	Metabolic Acidosis	n=12 42.9%	n=16 57.1%

	Normal pH	n=45 88.2%	n=5 11.8%
	Respiratory Alkalosis	n=8 100%	n=0

(P Value = 0.0001)

The three variables namely, clinical severity, need of ventilatory support and the outcome had statistically significant correlation with pH.

5. ECG changes are classified into three groups (35)

ECG with normal limits n=22

Phase 1GROUP - n=43

Phase 2 GROUP n=18

Phase 3 GROUP n= 4

Out of 18 in phase 2 group of ECG changes seven needed ventilatory support and the morality rate was 33.34%(n=6).All the four cases in phase3 group needed ventilatory support and every one recovered.

6. Gastric aspirate analysis by Thin layer chromatography in detection of OPC.

In this series out of 75 cases of ingestional form of exposure the TLC method detection rate was 84 percent.

7. Pseudocholinesterase Levels in OP Poisoned Patients

Table 32 - Pseudocholinesterase Levels in OPC poisoned Patients

Serum CHe Level IU/L	N	Mean	SD	Minimum Value	Maximum Value	Range
Day 1	87	841.32	1426.7	31.00	7000.0	6969.0
Day 3	87	1301.7	1697.4	48.00	7259.0	7211.0
Day 5	87	1664.3	1965.7	50.00	7259.0	7840.0

The mean level of Serum CHe among the age and sex matched control population (n=46) is 7090 IU per litre. The total number of 87 patients were classified on the basis of serum CHe level in the following manner :

1. Mild (20 to 50% of 7090)

2. Moderate (10 to 20% of 7090) and

3. Severe (Less than 10%)

In these series, Day 1 CHe estimation correlated well with Dreishbach clinical criteria of severity but it has no statistically significant relationship to predict the need of mechanical ventilation and outcome.

Table 33 – Day 1 Serum AcHE Level & Clinical Severity

Day 1 Serum CHe Level as % of Normal	Clinical Severity		
	Mild	**Moderate**	**Severe**
Normal (>50%)	n=2 50%	n=2 50%	n=0
Mild (20 to	n=2 20%	n=6 60%	n=2 20%
Moderate (10 to	n=5 50%	n=0	n=5 50%
Severe (≤10	n=6 9.5%	n=21 33.3%	n=36 57.1%

(P value = 0.00167)

Day 3 and day 5 serum CHes estimation had significant and very significant statistical relationship respectively with three variables of clinical severity, to predict the need of mechanical ventilation and outcome.

Table 34 - Day 3 Serum AcHE Level & Clinical Severity

Day 3 Serum CHe Level as % of Normal	Clinical Severity		
	Mild	**Moderate**	**Severe**
Normal (>50%)	n=6 60%	n=4 40%	n=0
Mild (20 to	n=2 14.3%	n=4 28.6%	n=8 57.1%
Moderate (10 to	n=3 20%	n=8 53.3%	n=4 26.7%

	Severe (<10)	n=4 8.3%	n=13 27.1%	n=31 64.6%

(P value = 0.00043)

Table 35- Day 3 Serum AcHE Level & Ventilatory Support

Day 3 Serum CHe Level as % of Normal	Ventilatory Support No support SIMV Mode	Assist Control Mode	
Normal (>50%)	n=10 100%	n=0	n=0
Mild (20 to 50%)	n=8 57.1% |	n=6 42.9%	n=0
Moderate (10 to 20%)	n=11 73.3%	n=4 26.7%	n=0
Severe (<10	n=16 33.3% |	n=29 60.4%	n=3 6.3%

(P value = 0.00311)

Table 36 - Day 3 Serum AcHE Level & Outcome

Day 3 Serum CHe Level as % of Normal	Outcome Discharge	Death
Normal (>50%)	n=10 100%	n=0
Mild (20 to 50%)	n=12 85.7% |	n=2 14.3%

	Moderate (10 to 20%)	n=13 86.7%	n=2 13.3%
	Severe (<10%)	n=30 62.5% |	n=18 37.5%

(P value = 0.02668)

Table 37 -Day 5 Serum AcHE Level & Clinical Severity

Day 5 Serum CHe Level as % of Normal	Clinical Severity		
	Mild	**Moderate**	**Severe**
Normal (>50%)	n=6 50%	n=6 50%	n=0
Mild (20 to 50%)	n=2 11.1% |	n=6 33.3%	n=10 55.6%
Moderate (10 to [illegible])	n=4 17.4%	n=12 52.2%	n=7 30.4%
Severe (<10 [illegible])	n=3 8.8% |	n=5 14.7%	n=26 76.5%

(P value = 0.00006)

Table 38 - Day 5 Serum AcHE Level & Ventilatory Support

Day 5 Serum CHe Level as %	Ventilatory Support		
	SIMV	**No support**	**Assist Control**
Normal (>50%)	n=12 100%	n=0	n=0

	Mild (20 to 50%)	n=10 55.6% |	n=8 44.4%	n=0
	Moderate (10 to 20%)	n=14 60.9%	n=7 30.4%	n=2 8.7%
	Severe (<10%)	n=9 26.5% |	n=24 70.6%	n=1 2.9%

(P value = 0.00044)

Table 39 - Day 5 Serum AcHE Level & Outcome

Day 5 Serum CHe Level as % of Normal	Outcome		
		Discharge	**Death**
	Normal (>50%)	n=12 100%	n=0
	Mild (20 to 50%)	n=17 94.4% |	n=1 5.6%
	Moderate (10 to 20%)	n=19 82.6%	n=4 17.4%
	Severe (<10%)	n=17 50% |	n=17 50%

(P value = 0.00021)

Table 40 - Creatine kinase (CK) and its MB Fraction (CKMB)

Sl.No.	Values	Normal	Mean	S.D. (+/-)
1.	CPK IU/L	15-130	723.20	827.75
2.	CPK MB IU/L	0-24	100.33	112.73

(P Value = 0.0000)

Both the enzymes level elevation in the cases of OP Compound poisoning were statistically significant.

Both serum CK and CK MB fraction elevation correlated very well with clinical severity grading and the need of mechanical ventilation. There is no statistical significant relationship between these enzymes elevation and the outcome.

Table 41 - Serum CK Level & Clinical Severity

Serum CK Level		Clinical Severity		
		Mild	**Moderate**	**Severe**
	Normal	n=5 38.5%	n=8 61.5%	n=0
	Abnormal	n=10 13.5%	n=21 28.4%	n=43 58.1

(P value = 0.00050)

Table 42 - Serum CK Level & Ventilatory Support

Serum CK Level	Ventilatory Support		
	SIMV	**No support**	**Assist Control**
Normal	n=13 100%	n=0	n=0
Abnormal	n=32 43.2% |	n=39 52.7%	n=3 4.1%

(P value = 0.00080)

Table 43 - Serum CKMB Level & Clinical Severity

Serum CKMB Level	Clinical Severity		
	Mild	**Moderate**	**Severe**
Normal	n=6 37.5%	n=9 56.3.5%	n=1 6.3%
Abnormal	n=9 12.7%	n=20 28.2%	n=42 59.2%

(P value = 0.00051)

Table 44 - Serum CKMB Level & Ventilatory Support

Serum	Ventilatory Support		
	No support	**Assist Control**	**SIMV**

	Normal	n=14 87.5%	n=2 12.5%	n=0
	Abnormal	n=31 43.7% |	n=37 52.1%	n=3 4.2%

(P value = 0.00642)

SERUM AMYLASE

In all 87 cases, serum amylase and ultra sonogram of the abdomen were done. Sonography of the abdomen were normal in all cases. The mean serum amylase level in the series 110 U/L. The rise of serum amylase levels was directly related to the severity and the need of mechanical ventilation.

Table 45 - Serum amylase Level & Clinical Severity

Serum amylase Level		Clinical Severity		
		Mild	**Moderate**	**Severe**
	Normal	n=11 22.9%	n=19 39.6%	n=18 37.5%
	Abnormal	n=4 10.3%	n=10 25.6%	n=25 64.1%

(P value = 0.04209)

Table 46 - Serum Amylase Level & Ventilatory Support

Serum Amylase Level		Ventilatory Support		
		No support	Assist Control	SIMV
	Normal	n=33 68.8%	n=15 31.3%	n=0
	Abnormal	n=12 30.8% |	n=24 61.5%	n=3 61.5%

(P value = 0.00087)

SERUM LDH

The mean LDH level in the series – 540 U/L (SD- (+/-) 247.02)

The Serum LDH elevation in cases of OPC poisoning was highly significant (P value = 0.0000). The LDH elevation did not have any correlation with clinical severity, need of mechanical ventilation and the outcome.

TREATMENT CONTRIBUTES

In our series of 87 patients mean atropine requirement: 268.51mg (S.D179.96) 2PAM was given to all patients. They were grouped in a non random fashion into two groups as low dose and high dose on basis of total dose given per day.(<4gm/day and >4gm/day). Average mean requirement of 2PAM - 31.64gm (SD 18.62|)36 patients came under the low dose group and 51 patients in the high dose group. These groups were compared in relation to severity, need of ventilatory support and outcome and their correlation was statistically significant.

Table 47 - 2PAM & Clinical Features

		Clinical Features		
		Mild	**Moderate**	**Severe**
2PAM	Low Dose	n=10 27.8%	n=16 44.4%	n=10 27.8%
	High Dose	n=5 9.8%	n=13 25.5%	n=33 64.7%

(P value = 0.00242)

Table 48 - 2PAM & Ventilatory Support

		Ventilatory Support		
		No Support	**Assist Control**	**SIMV**
2PAM	Low Do	n=30 83.3%	n=5 13.9%	n=1 2.8%
	High Dose	n=15 29.4%	n=34 66.7 %	n=2 3.9%

(P value = 0.0000)

Table 49 - 2PAM & Outcome

		Outcome	
		Discharge	**Death**
2PAM	Low Dose	n=32 88.9%	n=4 11.2%
	High Dose	n=33 64.7%	n=18 35.3%

(P value = 0.01059)

VENTILATORY SUPPORT

Out of 87 patients 42 needed ventilatory support.(48.27%).39 patients were initiated on assist control mode and three were started on simv mode.

The average duration of mechanical ventilation in the series was 7.11days (S.D= 4.53) .The more the severe grade of poisoning more was the need of mechanical ventilation.(pvalue=0.0000).19 out of 42 cases on mechanical ventilaton expired .The morality rate among patients on mechanical ventilation was 45.23%. Their correlation was very significant. The mortality rate differed with patients with ventilatory support and with that of no support (6.7%). The difference was statistically significant.

Table 50 - Ventilatory Support & Outcome

	Ventilatory Support	No Support
No.of Patients	42	45
Recovered	23	42
Expired	19	3

(P Value =0.001)

All the 8 cases of IMS (type2)syndrome were on mechanical ventilation.The mean duration of these cases on mechanical ventilation-17.5 days. One case expired and seven got discharged.Eight cases needed tracheostomy during mechanical ventilation and three cases out of them had type2paralysis.

Outcome In this series 22 expired. The mortality rate was 25.29%. In 18 cases primary cause of death was respiratory failure with secondary cardiac arrest.

It has resulted from central respiratory depression, respiratory muscle weakness, increased bronchial secretions, broncho spasm and acute pulmonary oedema.4 cases developed torsades de pointes and they expired due to ventricular fibrillation.19 out of 22 cases needed ventilatory support.

LOGISTIC REGRESSION ANALYSIS

in order to identify important variables that would predict the need of mechanical ventilation and outcome this stastical method was adopted.

a**. Need for ventilatory support**

Dependant variable – ventilatory support.

Independent variables- 1.Duration of hospital stay

2. Clinical severity grading

3. Proximal muscle affection

4.Creatine kinase (CK)

5.Total dose of atropine(mg)

6.Day 1serum AcHE level

7.Total dose of 2PAM

The correlation was found out to be very significant (p=0.0000) by chi square test. The prediction percentage was high as 96.55%.

INFERENCES: Variables with positivity were clinical severity,total dose of atropine and total dose of 2PAM, ie more the clinical grade of severity, greater the dose of atropine and 2PAM the need for mechanical ventilation was high.

Variables with negativity were duration of hospital stay, proximal muscle affection, day1 serum ChE and creatine kinase (i.e.) shorter the hospital stay, non involvement of proximal muscle group, lesser inhibition of day 1 serum che and low creatine kinase the need for ventilatory support was low.

B PREDICTORS OF.OUTCOME

Dependant variable-Outcome

Independent variables

1.Duration of hospital stay

2.Clinical severity grading

3. Proximal muscle affection

4.Creatine kinase (CK)

5.Day 1serum AcHE level

6.Day 5serum AcHE level

7. Total dose of atropine

8.Total dose of 2PAM

9.Ventilatory support.

The correlation was found out to be very significant($p=0.0000$) by chi square test. The prediction percentage was 87.36%.

INFERENCE: Patients with severe poisoning (driesch bach criteria), elevated levels of creatine kinase, more the total dose of atropine , greater reduction of day 1 che levels were associated with significant mortality.

In the series, patients with shorter duration of stay in the hospital,noninvolvement of proximal muscles, lesser inhibition of day 5 che levels and lower the dose of total p2am administered were associated with good outcome,.

DISCUSSION

Comprehensive analysis of 87 cases of acute organophosphorous poisoning

EPIDEMIOLOGY OF ORGANOPHOSPHOROUS POISONING:

Age Pattern.

In this series the opc poisoning was prevalent in the 21-30 age group.57cases were below the age of 30.WHO has reported about 3million cases of opc exposureand40,000deaths annually and majority were under the age group of thirty. (36) Murat Sungur and Muhammed Güven et al of TURKEY observed the mean age group of opc exposure was 30±15 years.(12) **Karalliedde L**, **Senanayake N**.et al of SRILANKA documented 91% of their cases were under the age of 30.(37). In Kashmir valley **Malik et al.** revealed that 33.5% of the cases of opc were under the age of 25.(38) In Mangalore, Karnataka, India the most common age group to be affected was between 20-30 (36.6%) (36). The series reported in this thesis had the similar pattern of age group affection. The reason could be that this age group by all probability is vulnerable to various emotional conflicts that occur during this phase of life. This young age group affected by exposure form the viable entity of any population both in terms of procurement and productivity. This case study and the case reports mentioned above throw light on the target age group for educative and preventive programmes to reduce the incidence of opc poisoning.

SEX DISTRIBUTION

In poison centre GGH Chennai males were exposed more when compared to female population.(87.36% versus 12.64%). On the contrary to the series in Murat Sungur study of 47 cases of opc in Turkey(12) [(female n=25, male=22)]and. **Malik et al.** observation of 122 cases in Kashmir valley[(female n=114,male=50)] female intoxication was more. In Srilanka and Mangalore had similar pattern to the case series of the poison centre.(male 86%-female 14%).S.Shivakumar and K.Raghavan et al of Tamil Nadu reported 165 cases of organo phosphorous poisoning and sex distribution was similar to the case series (male n=122, female n=45)(39).This variation was due to handling of poison by the respective sex in their respective locality. In Kashmir the female population are predominantly employed in apple orchards and they are involved in pesticide control. In southern part of India males are actively involved in spraying fertilizers and pesticides.

OCCUPATION AND SOCIOECONOMIC STATUS

Wesselling C, **McConnell R, Partanen T**, **Hogstedt C** et al reported that large worker populations in the Third World were exposed to increasing amounts of pesticides, including pesticides severely restricted and banned in industrialized countries. Studies on knowledge, attitudes, and practices indicate that unsafe use of pesticides was the rule in Third World countries.(40).In our case series 77out of 87 cases were agriculturists and unskilled labourers.54.02% of the cases were from rural areas.(n=47).The mortality rate were also high among the these group.

In Kashmir valley two third of the population who had exposure were engaged in apple orchard.In Karnataka agriculturists formed the majority.Students formed the predominant group in Nepal (41) whereas in Almeria exposure was more in green house workers.(42).

INTENTION OF POISON.

Estimates from the WHO indicate that each year, 1 million accidental poisonings and 2 million suicide attempts involving pesticides occur worldwide. (10). In the series majority of cases were suicidal in nature which was consistent with other workers.75cases(86.21%) were suicidal and 12 cases(13.79%) had accidental exposure.

Murat Sungur and Muhammed Güven et al observed 68%of opc poisoning reported were of suicidal exposure and Karalliedde L, Senanayake N et al of SRILANKA had similar pattern. Malik et al. reported 74.4% of cases were of suicidal in nature and rest(25.6%) had accidental exposure. Palimar Vikram MD**,** Arun M MD, DNB et al in their case study of 153 cases in Mangalore reported 98.7%of sucidal exposure. Most of the agriculturists consume for the fact of failure of crops, increasing debts coupled with the easy availability of poison.

2700 people are referred to hospital for self poisoning each week in the United Kingdom alone. It is likely to be even more difficult for the developing world, with its limited resources, to address this problem effectively. However, we

think that the time has come to acknowledge the seriousness of the situation as a first step towards preventing this massive unnecessary loss of life.(43)

ROUTE OF EXPOSURE:

Ingestion of the opc poisoing (n=75) formed th majority in this series apart of inhalational(n=10) and topical (n=2) form of exposure.

In the series most cases of grade III severity were ingested OPC but the correlation with the outcome was not significant. The mortality rate in the ingestional group-26.7% Arup Kumar Kundu, JD Mukhopadhyay**,** AK Saha, S Das et al(44)studied 108patients in sub urban West bengal poison.90 consumed the poison and the death rate was12% and it had positive correlation with outcome. In Kashmir Valley out of 164 cases-ingestional route(n=140), inhalational (n=7) and topical exposure(n=17). In the Turkey study the gastrointestinal route was the main route in 44 (93.6%) patients.

TYPE OF POISON

In this study parathion(34.49%) and dimecron(29.89) were the most common type of poison consumed when compared to other workers. The type of poison did not contribute much to the severity and mortality.

Murat Sungurb et al in TURKEY observed the three common type of opc were:

Agent	Number of patients
Dichlorvos	24 (51.1%)
Ethyl-Parathion	5 (10.6%)
Fenthion	4 (8.5%

In sub urban West Bengal Arup kumar kundu et al showed that mortality was high in poisoning with monocrotophos and dimethoate (31%) and nil with malathion. In the Mangalore study methyl parathion was the most common poison consumed. Karalliedde L, Senanayake N. reported dimethoate, methamidophos, malathion, monocrotophos and fenthion as the common type opc consumed in Srilanka. In the Kashmir valley phosphamidon(55%), malathion(12%) and dichlorovas(8.5%) were the commonly used opc compounds for ingestion.In study from Tamil nadu S.Shiva Kumar and K.Raghavan et al of Tamil Nadu reported methyl parathion as the most common form of exposure in their study group.

In this case series the severity of poison was directly proportional to quantity consumed. (pvalue=0.004).There was no relation to mortality. But the study from West Bengal showed there was a correlation between the quantity consumed and the mortality.

CLINICAL CONTRIBUTES

In this case study, the average duration between the onset of symptoms and consumption was 44.73 (SD 26.76). Dr.Sumathi Joshi et.al. reported that the symptoms of OPC poisoning developed between 30 minutes and 1 hour (45). In this study group, patient reaching the Poison centre by more than 6 hours had grade 3 severity (P value 0.02). More than 60 per cent of the cases have the accessibility to have their first aid, first doses of atropine and 2PAM before 3 hours. But these variables did not have significant correlation with the outcome. But the West Bengal workers reported increased mortality among the patients who had increased time interval before initial atrophinazation (44). In this series, presenting muscuranic symptom predominantly involved the GIT (68%) followed by the central nervous system manifestations. Murat Sungurb et al in Turkey reported that the CNS symptoms such as depressed mental status, confusion and muscle weakness were the common presentation. Kenneth D.Ketz et.al. from Pittsburg reported neuro psychiatric manifestations, ototoxity, Guillain-Barré (46) –like syndrome and isolated bilateral recurrent laryngeal nerve palsy in OPC poisoning. In this series, there were two cases with lower cranial involvement, one with bilateral LMN type of facial palsy and the other with tenth cranial nerve affection.

CLINICAL SEVERITY (MODIFIED DREISHBACH CRITERIA)

In this case series, most of the patients admitted fell into the grade 3 group of clinical severity (n=43) 49.4%. The reason could be that this centre being a referral unit, complicated cases, warranting specialist treatment, intensive care monitoring, ventilatory support (n=65) were transferred from primary health centres, district hospitals and private nursing homes. Arup Kumar Kundu (et.al) reported, mild 15 (14%), moderate 55 (50.9%), and severe 32 (29.6%) in his study based on OPC poisoning in sub-urban West Bengal. In that study, the severe grade of poisoning was associated with increased ventilatory support and poor outcome. Similarly, in this case series, clinical severity association with need of ventilatory support and mortality was statistically significant (P value = 0.002).

In this case study, proximal muscle group affection formed an important parameter to assess the need of ventilatory support, progression to grade 3 severity and predictor of outcome.

LAB CONTRIBUTES

In this study group, the average total WBC count 14,038 cells cubic mm. (SD. 5233). Leucocytosis were also reported in the studies from Turkey and Pittsburg. The liver function tests observed in this study had similar pattern of mild elevation when compared to the study from Murat Sungurb et al in TURKEY. The arterial blood gas analysis performed in this study had significant correlation with severity, outcome and the need of ventilatory support similar to

the observations made by A.Goe, S.Joseph, et.al.(47). Kenneth D. Ketz, et.al. who documented metabolic acidosis in his study group.

ECG

Most of the cases in this series had sinus tachycardia (n=43) 18 cases had AV nodal inhibition and 4 cases had QT_C prolongation followed by torsade de pointes, ventricular tachycardia and ventricular fibrillation. Patients with phase 2 and phase 3 ecg changes as described by Ludomirsky et al. (25) were associated with grade 3 severity and outcome similar to observations made by Dalvi, CP, et.al.(48).

CHOLINESTERASE LEVELS AND ITS SIGNIFICANCE

In this case study, day 1 Che correlated very well with clinical criteria of dreishbach (P value = 0.001). This finding was also observed by Bobba R, Venkataraman, BV, Pais P, Joseph T. et.al. in Bangalore (49). In contrary to this observation, S.N. Chugh and Navneeth Agarwal, et.al. found no relationship between serum CHE estimation and severity grading (50). In this case series, logistic regression analysis was run to predict the outcome in which day 1 and day 5 CHE level were important parameters. Sequential post exposure estimations of the ChEs upto 5 days not reveal any rise in the values though there was substantial clinical improvement. This observation was in par with the study in Bangalore (49). Day 3 and day 5 ChE levels in this study had statistically significant association with need of ventilatory support.

SERUM AMYLASE

In all 87 patients serum amylase and ultra sonogram of the abdomen was performed in order to identify transient pancreatits which is a rare complication (51). Ultra sonography of the abdomen was done in all the cases. Serum Amylase elevation was statistically significant. 4 cases out of 87, had serum amylase level > 300 U/L out of which two cases expired. Sahin I, Onbasi K, Sahin H, Karakaya C, Ustun Y, Noyan T. et.al. observed 4 out of 47 cases in their series, had amylase elevation more than 300 U/L.(52). Lee WC, Yang CC, Deng JF, Wu ML, Ger J, Lin HC, Chang FY, Lee SD, et.at. stated that : hyperamylasemia was frequent in severe organophosphate poisoning. However, hyperamylasemia was not synonymous with acute pancreatitis and pancreatic amylase was not a reliable parameter in the diagnosis of organophosphate-induced pancreatitis due to its low sensitivity and specificity (53). In this series of 87 patients in Poison centre serum amylase level was directly related to clinical severity and the need of ventilatory support (P value < 0.001). This observation was also documented in the Taiwan study (53).

SERUM LDH

Serum LDH elevation denotes oxidative damage done to skeletal muscles during OPC. (55). In this series, mean LDH levels were 540.53 U/L (SD 247.02) and the elevation was significant. Murat Sungur and Muhammed Güven of Turkey observed mean LDH levels of 548.8 ± 45.5 U/L. Sahin I, Onbasi K,

Sahin H, Karakaya C, Ustun Y, Noyan T. et.al. also found out LDH levels to be elevated. But in this series, LDH did not have any correlation with clinical severity, outcome nor to the need of ventilatory support.

CK AND CK MB

In this series, both enzyme level elevation were significant. CK rise may indicate skeletal muscle injury due to sustained stimulation of acetylcholine at the neuro muscular junction. The MB fraction of CK suggest myocardial dysfunction due to primary effect of OPC compounds on the heart as well as overzealous administration of atropine. Both CK and CK MB elevation were able to predict the clinical severity and the need of ventilatory support but not in outcome assessment. John M, Oommen A, Zachariah A. et.al. studied the correlation between muscle injury and Type 1/Type 2 paralysis with enzymes markers in OPC poisoning and made similar observations (54).

TREATMENT CONTRIBUTES

The average total dose of atropine administered in the case series, 268.51 mg (SD 179.96) Murat Sungur and Muhammed Güven of Turkey study of 47 patients their average total dose of atropine was 79.1 ± 62.9 mg. S.N. Chugh and Navneeth Agarwal, et.al. observed the average total dose for atropine 248 ± 196mg.

In this series, 2PAM was given to all patients.They were grouped in a non random fashion into two groups as low dose and high dose on basis of total dose

given per day.(<4gm/day and >4gm/day). Average mean requirement of 2PAM - 31.64gm (SD 18.62)came under the low dose group and 51 patients in the high dose group. The grade of clinical severity, the need of ventilatory support and the mortality were more among the high dose group when compared to the low dose administration of 2PAM. Arun Kumar Kundu, et.al. in a study in sub-urban West Bengal related high dose 2PAM administered in first 24 hours was associated with adverse outcome (44). In 1991, De Silva studied the treatment of organophosphate poisoning with atropine and 2-PAM and, later the same year, with atropine alone. He found that atropine seemed to be as effective as atropine plus 2-PAM in the treatment of acute organophosphate poisoning. The controversy continued when other authors observed more respiratory complications and higher mortality rates with use of high-dose 2-PAM. Low-dose (1-2 g slow IV) 2-PAM is the current recommendation. Studies are underway to assess the role of low-dose 2-PAM (39) A recent meta-analysis performed by Peter et al (2006) revealed that oxime therapy was associated with a ”null effect or possible harm” in terms of organophosphate poisoning (56). Johnson S, Peter JV, Thomas K, Jeyaseelan L, Cherian AM. et.al. in their double blinded randomized control study revealed high dose 2PAM group were associated with risk of intermediate syndrome, longer duration of ventilation and increased mortality rate (39) S.Shivakumar and K. Raghavan, et.al. compared the effectiveness of high dose 2PAM with low dose by selection of patients in non-random manner. They found out the high dose 2PAM group had better survival, lesser incidence of type 2 paralysis and shortened duration of ventilation.

VENTILATORY SUPPORT

Out of 87 patients 42 needed ventilatory support.(48.27%).39 patients were initiated on assist control mode and three were started on simv mode.19 out of 42 cases on mechanical ventilaton expired. The morality rate among patients on mechanical ventilation was 45.23%. The difference in mortality between the ventilatory and the non-ventilatory was significant (P value 0.00013)

The average duration of mechanical ventilation in the series was 7.11days (SD = 4.53). Grade 3 clinical severity, proximal muscle affection, elevation of creatinine Kinase, low values of day 1 serum ChE and higher dose of 2PAM were the predictors for the need of mechanical ventilation. Murat Sungur and Muhammed Güven of Turkey in the study of 47 patients of OPC reported Mechanical ventilatory support was needed for 10 (21.2%) patients The duration of mechanical ventilation was 4.1 ± 3.2 days. The mortality rate for the patients who were mechanically ventilated was 50% (5 patients), although the mortality rate was 27.6% (13 patients) for all patients. The mortality rate for the mechanically ventilated patients was not statistically different compared with those patients not mechanically ventilated. Two patients who are mechanically ventilated died with sudden cardiorespiratory arrest following ventricular tachycardia, and three died from pneumonia and complicating adult respiratory distress syndrome S.Shivakumar and K. Raghavan, et.al. in their case series of 165 patients 22 to patients were mechanical ventilated, out of which 14 died.

OUTCOME ANALYSIS

In this series 22 expired. The mortality rate was 25.29%. In 18 cases primary cause of death was respiratory failure with secondary cardiac arrest. It has resulted from central respiratory depression, respiratory muscle weakness, increased bronchial secretions, broncho spasm and acute pulmonary oedema.4 cases developed torsades de pointes and they expired due to ventricular fibrillation.19 out of 22 cases needed ventilatory support. By statistical method of logistic regression, the following parameters predict the outcome. The prolonged duration of hospital stay grade 3 clinical severity, proximal muscle involvement, suppressed day 1 and day 5 ChE levels, elevated creatine kinase, high dose of 2PAM and mechanical ventilation were associated with poor outcome. Karalliedde L, Senanayake N. et.al. reported mortality rate of 18% in their study of 92 cases of OPC in Sri Lanka. Arup Kumar Kundu, JD Mukhopadhyay, AK Saha, S Das Burdwan Medical College and Hospital, Burdwan, West Bengal analysed that increased time interval before initial atropinisation, higher clinical grading, respiratory paralysis at the time of admission, higher quantity of poison consumed, type of poison (e.g., monocrotophos and dimethoate), poison ingested rather than inhaled, development of encephalopathy and/or is ECG changes (pulse rate < 45/min, complete heart block QT-prolongation), and higher dosage of PAM used in first 24 hours were associated with increased mortality. In Kashmir valley a study of 164 patients of OPC poisoning, the mortality rate was 5.5%. In the Mangalore study, the mortality was 26.2%. Murat Sungur and Muhammed Güven of Turkey reported the mortality rate of 32%.

CONCLUSIONS

- Organophosphorous poisoning is most prevalent in the 21-30 age group.Incidence is more common in males .
- Organophosphorous poisoning is more common among agricultural labourers and unskilled workers.
- The most important cause for consumption of organophosphorous poison is self harm.
- The common route of exposure is ingestion of poison and it is associated with clinical severity.($p<.0.05$).
- The quantity consumed has direct proportional relationship with severity of poisoning($p<0.01$).
- The duration of stay in the hospital has significant correlation with clinical severity($p<0.01$)
- The higher the clinical grade of poisoning at initial presentation more the need of ventilatory support($p<0.01$) and adverse the outcome($p<0.01$)
- The proximal muscle involvement in organophosphorous poisoning forms an important indicator in assessment of clinical severity($p<0.01$),need of ventilatory support($p<0.01$) and the outcome.($p<0.05$).

- The day one serum cholinesterase level can be used as a diagnostic marker and a tool to gauge the clinical severity.($P<0.01$).

- The day three and day five serum cholinesterase level estimation has a strong prognostic value in assessment for the need of ventilatory support($p<0.01$)and outcome($p<0.01$).

- The blood gas analysis forms an important investigation in organophosphorous poisoning in correlation with clinical severity($p<0.01$),prediction of ventilatory support($p<0.01$) and the outcome.($p<0.01$)

- Serum creatine kinase and lactate dehydrogenase elevation are significant in organophosphorous poisoning($p<0.01$).They reflect skeletal muscle injury and oxidative stress caused by the poison.

- Serum creatine kinase and the MB fraction prove to be a prognostic indices in predicting the grade of clinical severity($p<0.01$) and need of ventilatoy support($p<0.01$).

- Hyperamylasemia is frequent in severe organophosphate poisoning.($p<0.01$) However, hyperamylasemia is not synonymous with acute pancreatitis of organophosphorous poisoniong.The enzyme elevation is directly related to severity($p<0.05$) and predicts the need of ventilatory support.($p<0.01$).

- The need of ventilatory support and the duration of mechanical ventilation are more for the high dose pralidoxime group($p<0.01$) when compared to the low dose group. Patients in the high dose pralidoxime group had adverse outcome.($p<0.01$).

- The following parameters predict the need of ventilatory support, grade 3 clinical severity, proximal muscle affection, elevation of creatine kinase, low values of day 1 serum cholinesterase and the high dose of pralidoxime. The parameters were evolved by statistical method of logistic regression with predictive percent of 96.55%.

- The following parameters predict the outcome. The prolonged duration of hospital stay, grade 3 clinical severity, proximal muscle involvement, suppressed day 1 and day 5 ChE levels, elevated creatine kinase, high dose of pralidoxime and mechanical ventilation are associated with increased mortality. The parameters were evolved by statistical method of logistic regression with predictive percent of 87.36%.

RECOMMENDATIONS AND AREAS OF FUTURE RESEARCH

1. In the management of organophosphorous poisoning the role of oximes is challenged by many studies(57).Hence a large high-quality RCT comparing the current WHO-recommended regimen with placebo is required to definitively assess the value of pralidoxime in acute OP poisoning.

2. Fresh frozen plasma therapy increases BuChE levels in patients with organophosphate poisonings. The administration of plasma may also prevent the development of intermediate syndrome and related mortality (58). Plasma (fresh frozen or freshly prepared) therapy may be used as an alternative or adjunctive treatment method in patients with organophosphate pesticide poisoning, especially in cases not given pralidoxime. Further randomized controlled are required to infer a definitive result.

3. Magnesium sulfate administration to cases of organophosphorous poisoning reduced mortality rate and decreased the duration of stay in the hospital (22).The role of magnesium sulfate need to be studied in our Indian context.

SUMMARY

Organophosphorous poisoning is a menace to the human race both as a weapon of mass destruction and a misused pesticide of self harm. The case fatality

rate exceed 60% in developing countries where there are many pit falls in treatment protocol and research activities. So a comprehensive analysis of 87 patients of organophosphorous poisoning was done in Poison Centre Government General hospital Chennai.

All the cases included in the studied underwent detailed clinical evaluation and extensive laboratory work up.Each patient was monitored periodically till the outcome. 47 intensive care unit. There were 76 males and 22 female patients. The predominant age group was 21- 30years.75 patients were suicide attempts and 12 had accidental exposure. 75 (86.2%) of the patients were poisoned through the gastrointestinal route. 10 (11.5%) patients had inhalational poisoning and two (2.3%) patients had topical exposure There were 12 different types of OP insecticide agents involved. The estimated average time for the admission to POISON CENTRE after the exposure was 9.9hours. According to Dreisbach clinical criteria at admission, 49.4% of patients belong to the severe grade of poisoning. 47 out of 87 cases had involvement of proximal muscles such as neck flexors, bulbar muscles and muscles of the shoulder and pelvic griddle. The blood gas analysis and serum cholinesterase levels had significant correlation with clinical severity,mechanical ventilation and outcome. Serum amylase, LDH, creatine kinase and ck-mb elevation were significant.

The average total dose of atropine was 268.51mg.All patients received pralidoxime. The grade of clinical severity, the need of ventilatory support and the mortality were more among the high dose group when compared to the low

dose group of patients who received pralidoxime. Mechanical ventilatory support was needed for 42(48.27%) patients

The duration of mechanical ventilation was 7.11 ± 4.5days. The mortality rate for the patients who were mechanically ventilated was 45.23%(19 patients), although the mortality rate was 25.29% (22 patients) for all patients. The mortality rate for the mechanically ventilated patients was statistically significant when compared with those patients not mechanically ventilated. The grade 3 clinical severity, proximal muscle affection, elevation of creatine kinase, low values of day 1 serum cholinesterase and the high dose of pralidoxime predicted the need of ventilatory support.

The predictors of adverse outcome were prolonged duration of hospital stay, grade 3 clinical severity, proximal muscle involvement, suppressed day 1 and day 5 levels serum cholinesterase ,elevated creatine kinase, high dose of pralidoxime and mechanical ventilation.

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PROFOMA - COMPREHENSIVE ANALYSIS OF ORGANOPHOSPHOROUS POISONING

NAME : AGE: SEX: OCCUPATION:

LOCALITY: D.O.A D.O.D

DURATION OF STAY : MORTALITY:

HISTORY

TYPE OF POISON

ROUTE OF EXPOSURE INGESTIONAL TOPICAL INHALATIONAL

QUANTITY

TIME OF ONSET OF POISONING

TIME OF INITISATION OF FIRST AID (LAVAGE ACTIVATED CHARCOAL)

TIME OF INITIATION of ATROPINE

TIME OF INITIATION of P2 AM

TIME TAKEN TO REACH HOSPITAL

ASSOCIATED POISONING
ASSOCIATED ALCOHOL INTAKE

SYMPTOMATOLOGY

INTENTION OF THE POISON: Suicidal Accidental Homicidal

CLINICAL CONTRIBUTES MILD No Symptoms; Normal vitals
Normal pupils

MODERATE
Fasciculation; Perspiration
Pupillary changes; Tachypnoea;
Early pulmonary edema

SEVERE
Pin point pupil, frank Pulm-edema ,
Respiratory paralysis, Unconciousness

PROXIMAL MUSCLE WEAKNESS:

BULBAR MUSCLE WEAKNESS:

NECK WEAKNESS:

IMS SYNDROME

ASSOCIATED CLINICAL FINDINGS:

LAB CONTRIBUTES

HEMOGRAM : HB TC DC ESR PCV

RFT Urea Creatinine Na+ k+ hco3 Cl-

SUGAR :

ABG : CXR: USG ABDOMEN:

ECG: ST-T CHANGES QTC PROLONGATION
LOW VOLTAGE PROGRESSIVE LOSS OF VOLTAGE

GASTRIC ASPIRATE

SERUM PSEUDO CHOLINEESTRASE LEVELS
DAY1
DAY2
DAY3

CPK CPK MB
LFT : SGPT SGOT SAP TB
LDH AMYLASE

TREATMENT CONTRIBUTES

TOTAL DOSE OF ATROPINE

TOTAL DOSE OF P2 AM (Less than 4 gms per day | More than 4 gms per day)

ANTIBIOTICS:TYPE DURATION

VENTILATORY SUPPORT: INTIATIONMODE:

DURATION :

OUTCOME

MORTALITY RATE

CAUSE OF DEATH

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Fig.3 Age Distribution

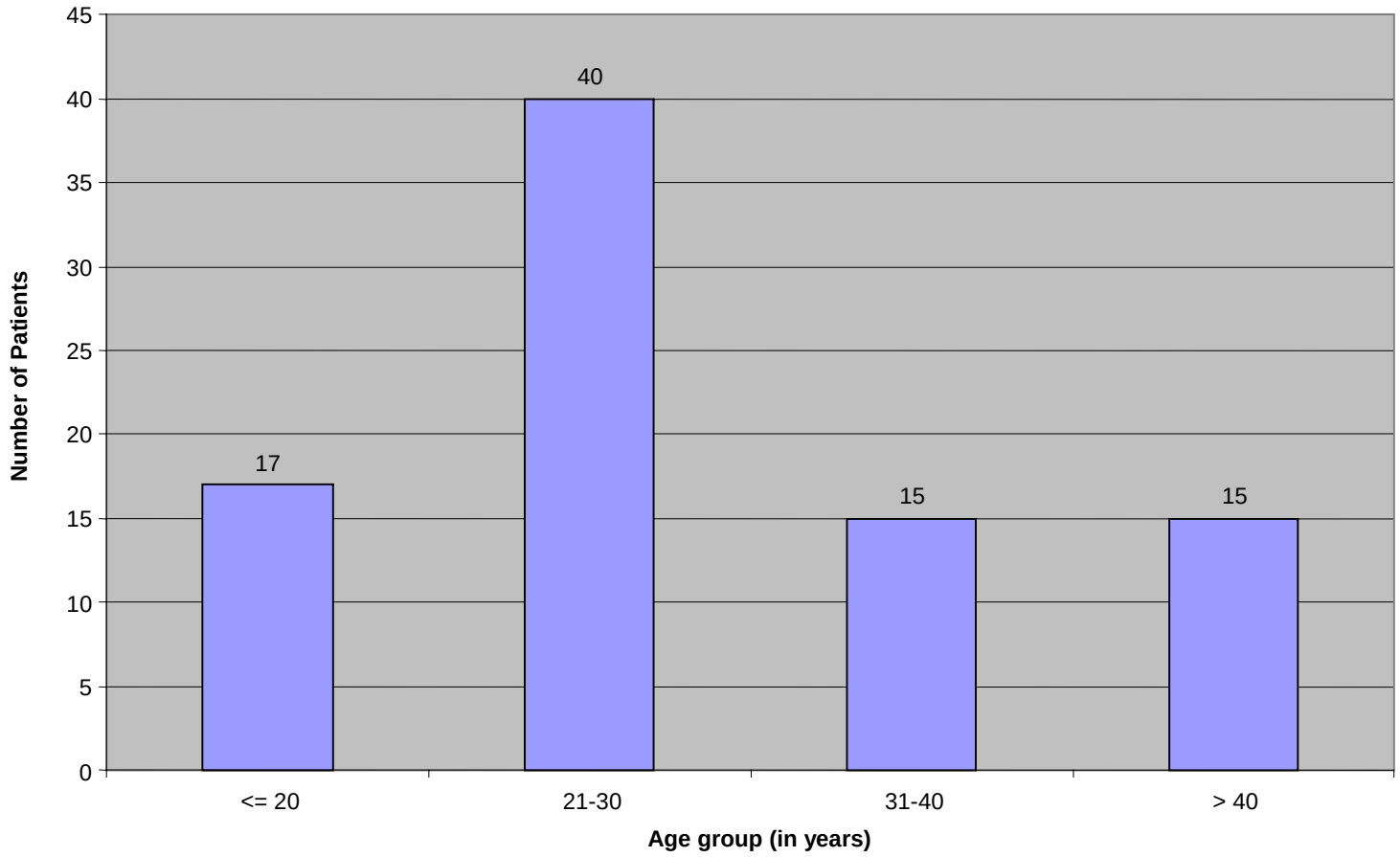


Fig.4 Sex Distribution

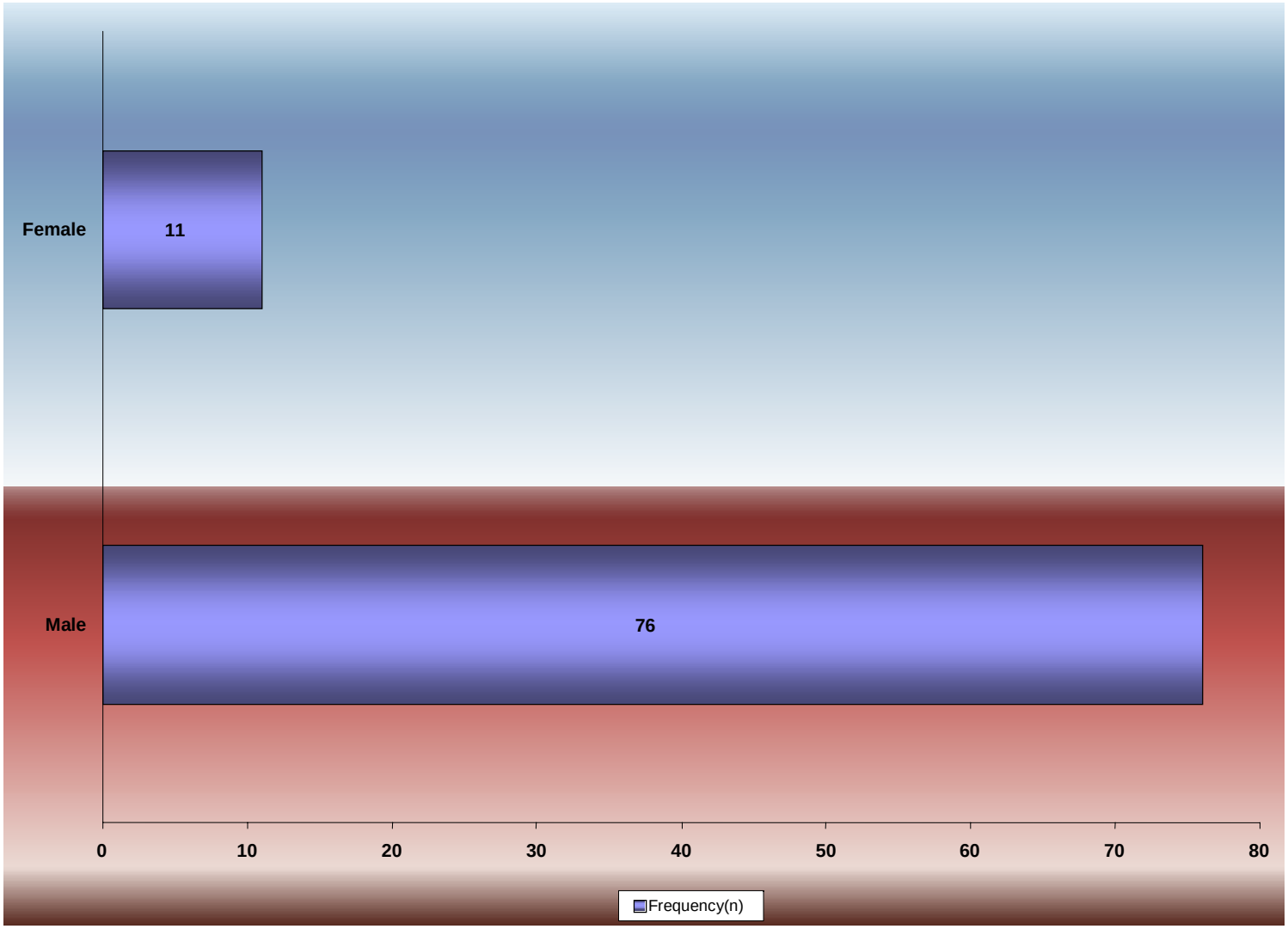


Fig.5 Occupation

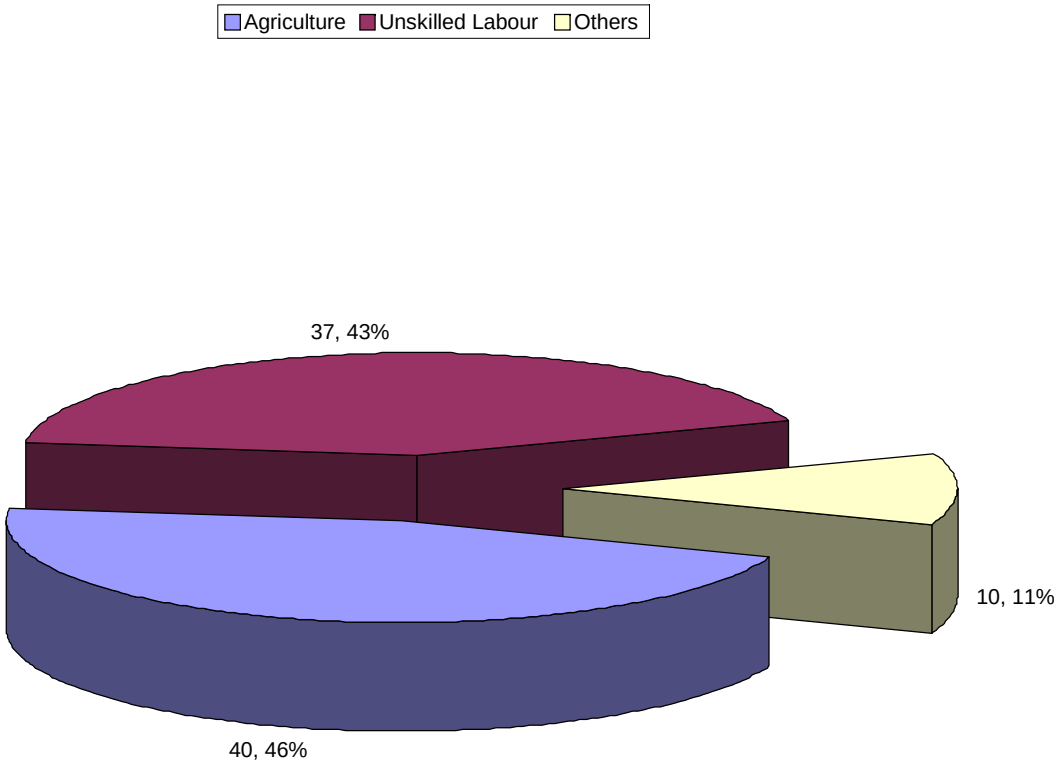


Fig. 6 Type of Poison

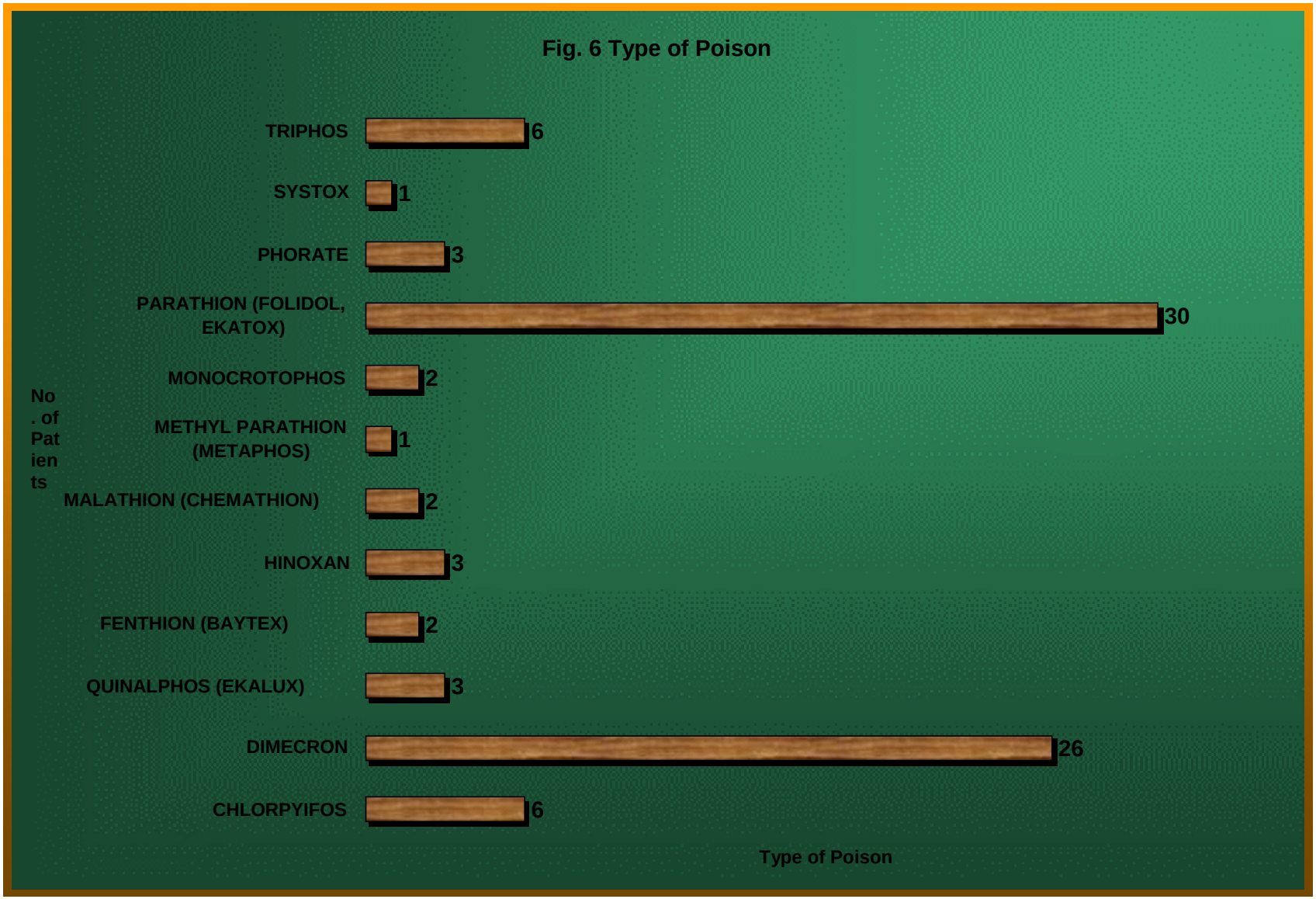


Fig.7 Route of

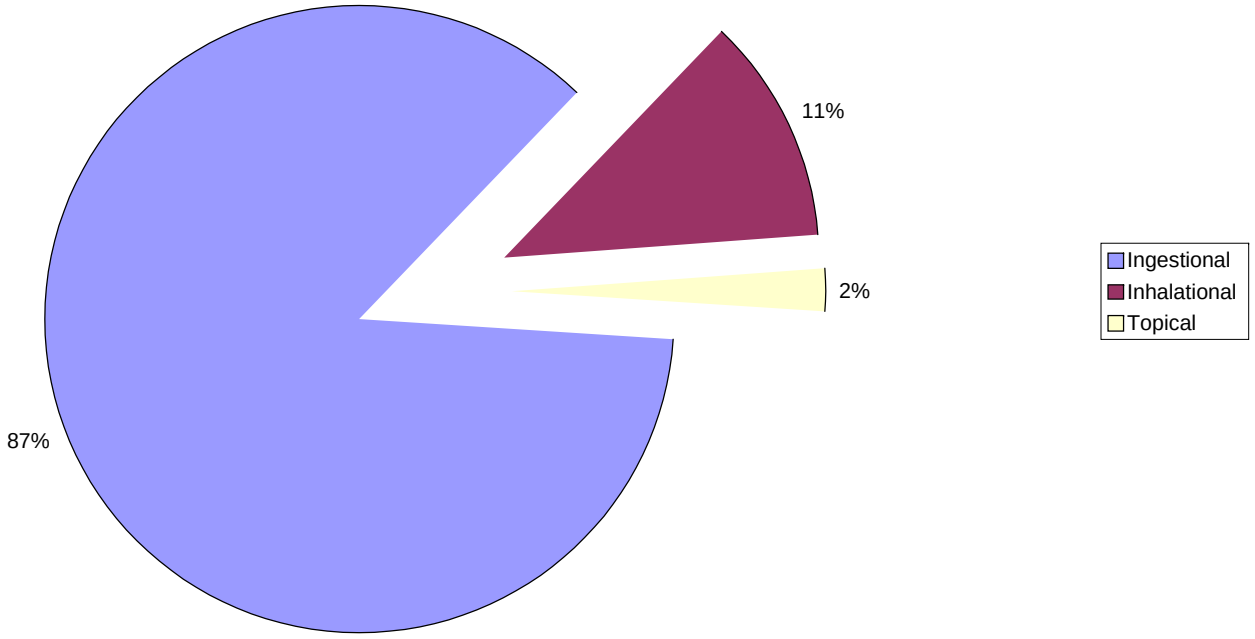


Fig.8 Quantity consumed

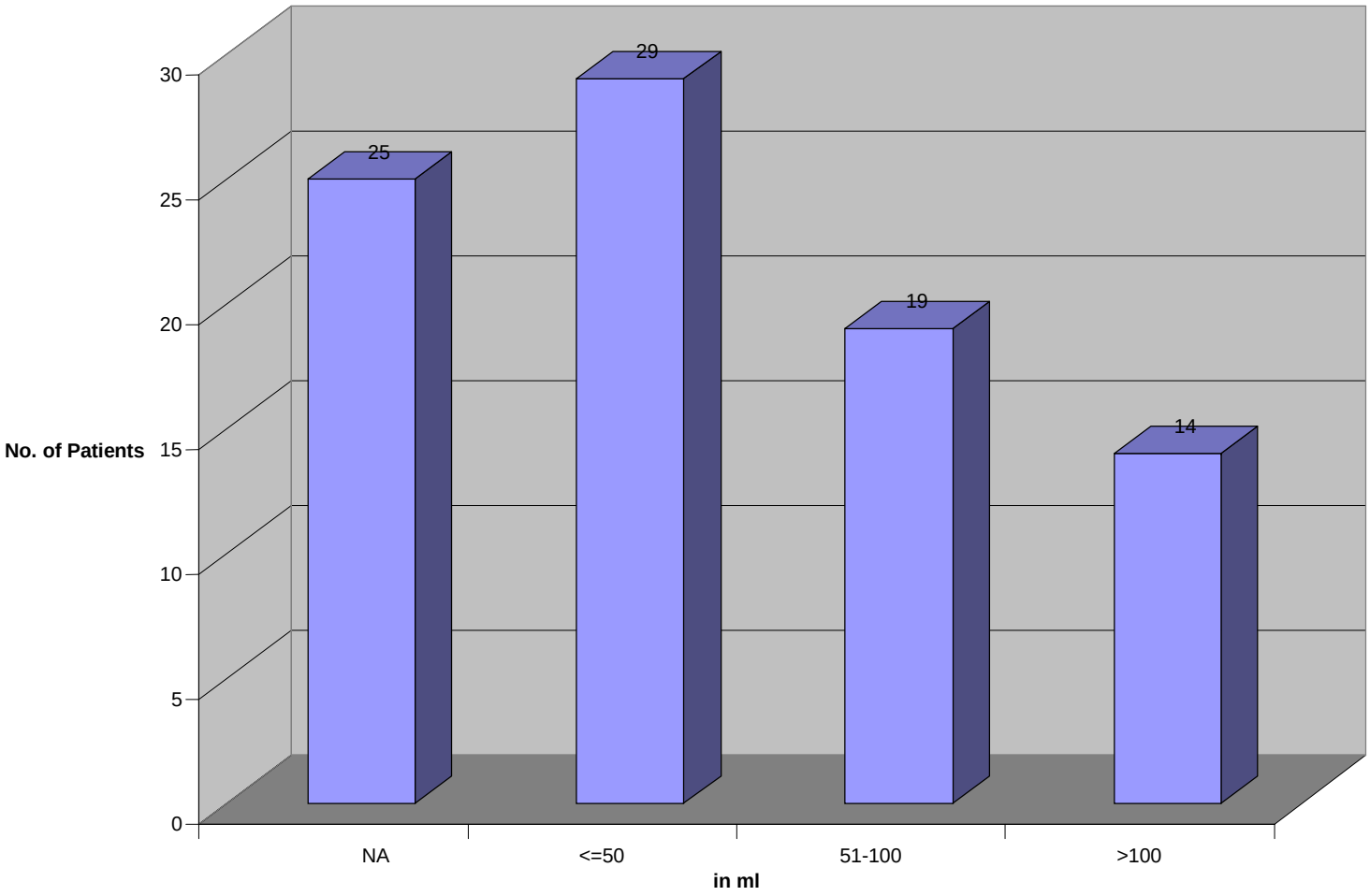


Fig.9 Dreischbach clinical criteria of

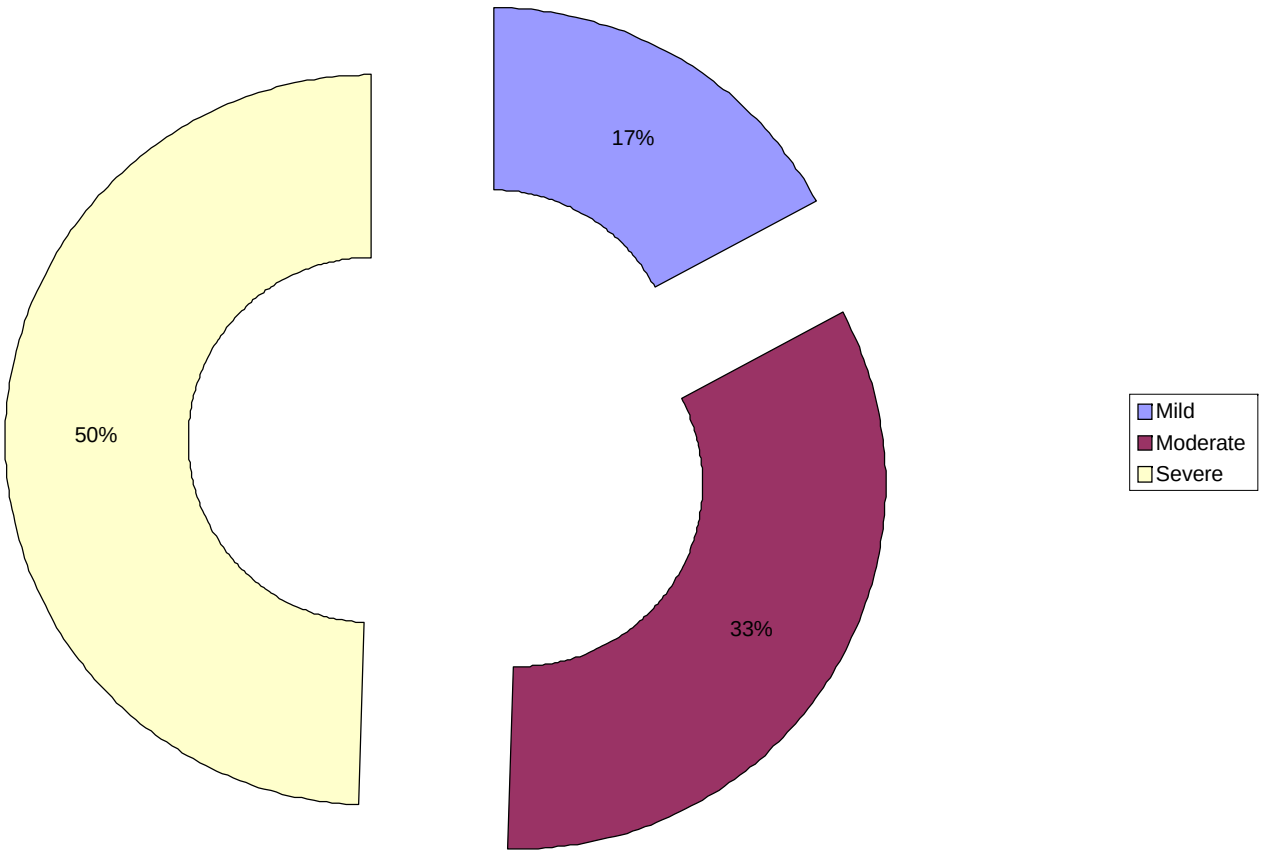


Fig. 10 Outcome

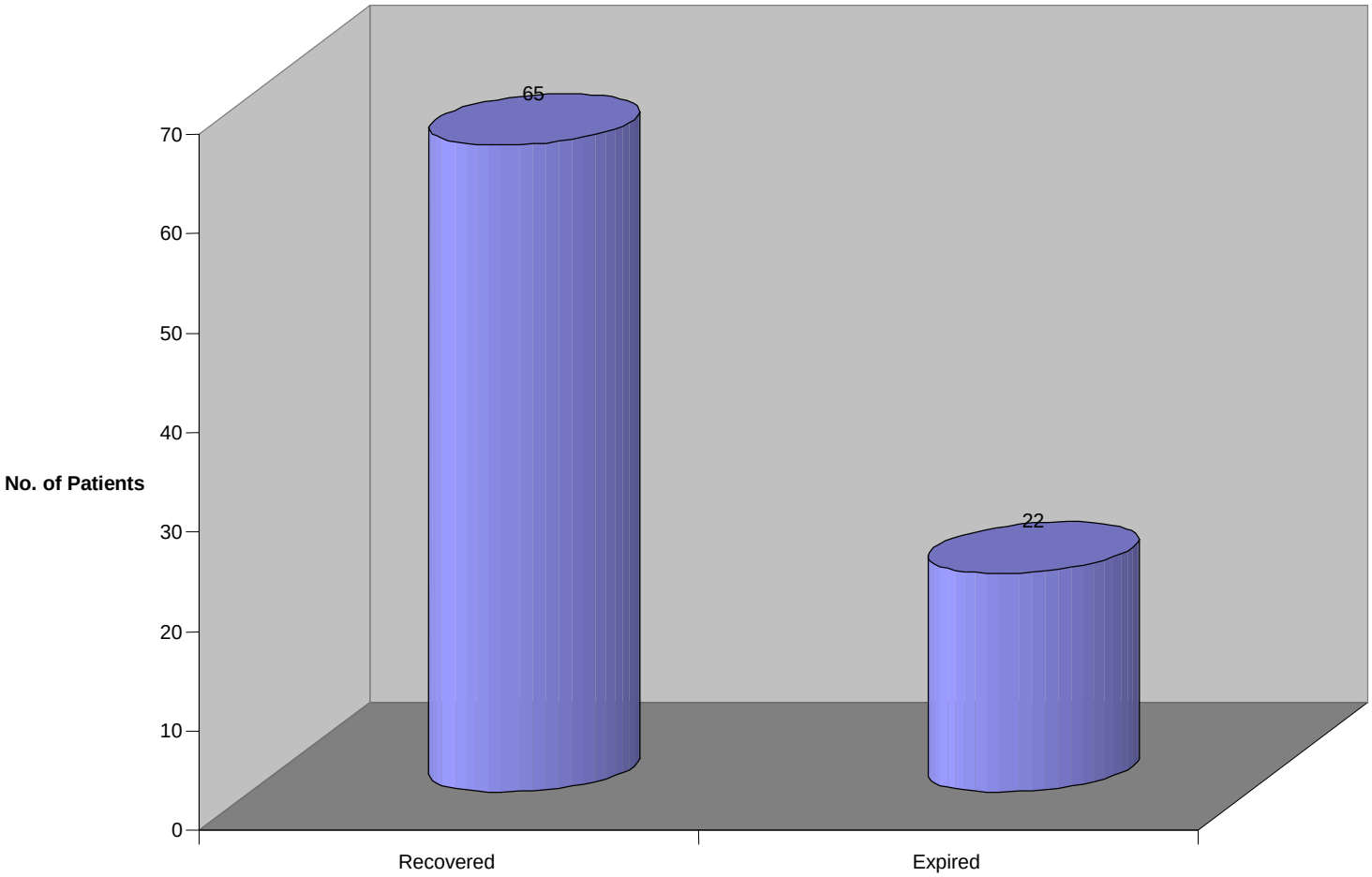
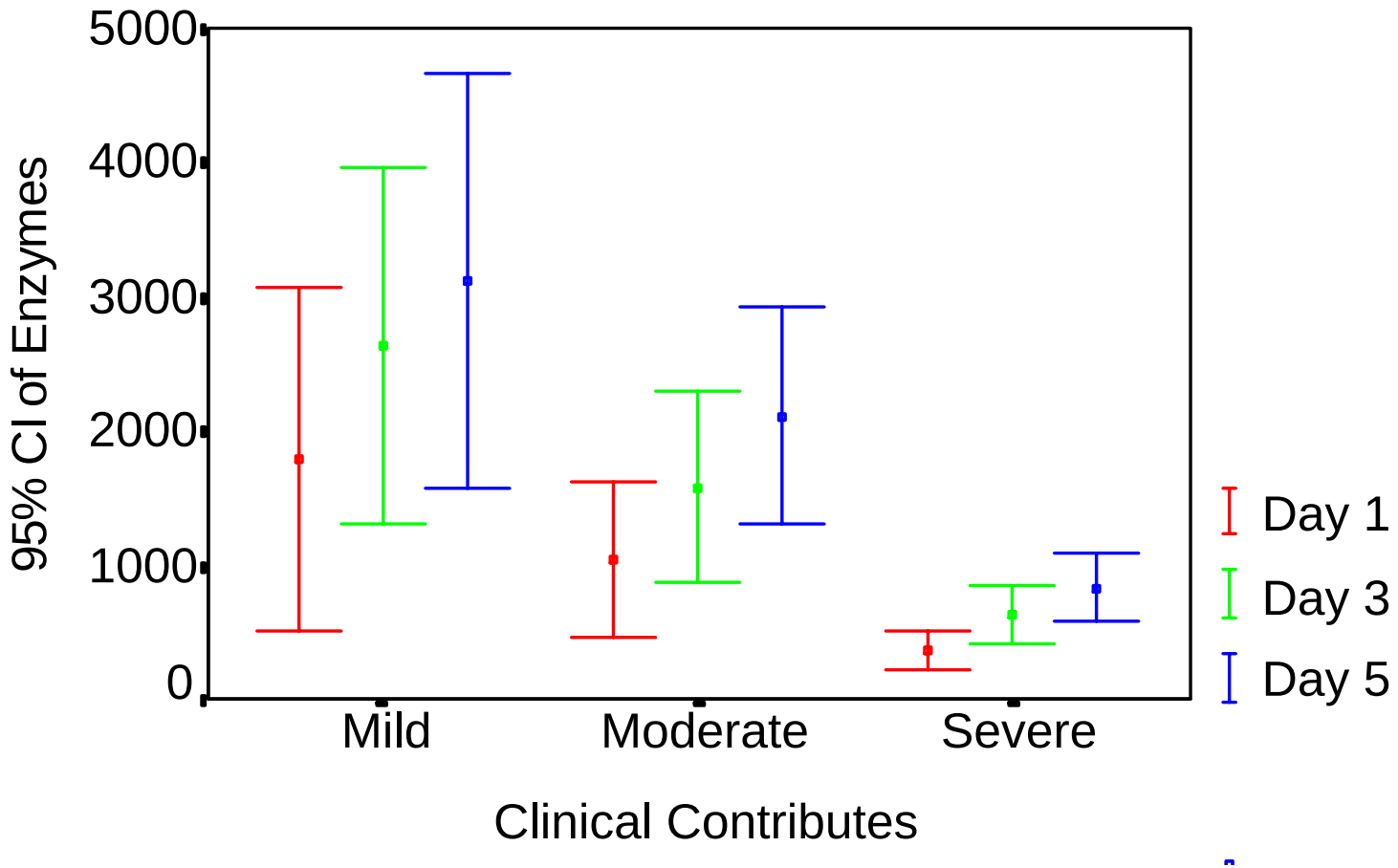


Fig.**11 Correlation of Serum Cholinesterase levels with Clinical grading**



KEY

Sex : Male = 1 Female = 2

Occupation : Agriculturist = 1 Unskilled workers = 2 Others = 3

Locality : <100 km = 1 >100 km =2

Intention : Suicide = 1 Accidental = 2

Association poison : Yes = 1 No = 2

Alcohol Intake : Yes = 1 No=2

Severity : Mild = 1 Moderate = 2 Severe = 3

Proximal muscle Involvement : Yes = 1 No.2

ECG : 1= PI 2=PII 3 = PIII 4 = Normal 5 = Sinus Bradycardia

Ventilatory support : 1=Nil 2=Assist Control 3 =Simv

Outcome : 1=Discharge 2 = Death